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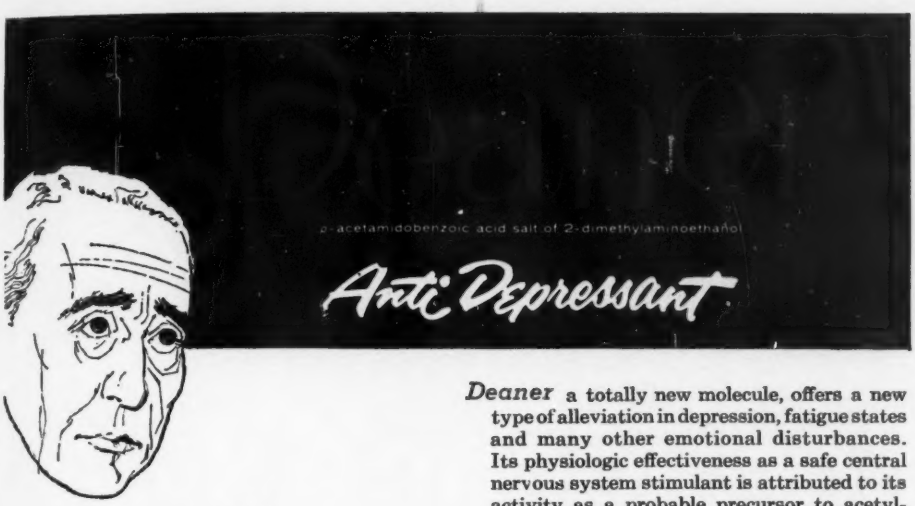
In Mild Depression



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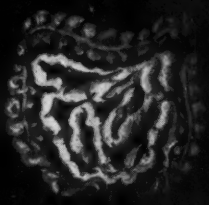

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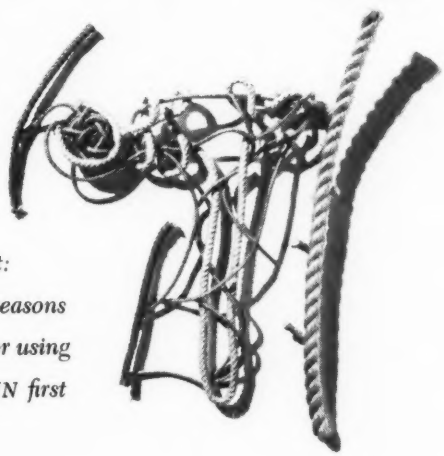

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Type of infection	Number of Patients	RESULTS Excellent to Good	Fair	Poor
Respiratory[3,4*]	32	32		
Shigella dysentery[5]	14	14		
Enteritis[5]	10	6	2	2
Bacteremia[3,5]	5	5		
Meningitis[3,5]	4	3		1**
Rocky Mountain spotted fever[3,5]	2	2		
Ear abscess with cellulitis[4]	1	1		
Lung abscess[4]	1			1
Typhoid fever[5]	1	1		
TOTALS	70	64	2	4

*Includes 15 patients who were administered CHLOROMYCETIN SUCCINATE by nebulization under intermittent positive pressure breathing.

**Patient was hydrocephalic at birth; cerebrospinal fluid was sterile at time of death.

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REFERENCES—(1) Glazko, A. J., *et al.*, in Welch, H., & Martí-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 792. (2) Unpublished data: Research Laboratories, Parke, Davis & Company, 1958. (3) Ross, S.; Puig, J. R., & Zaremba, E. A., in Welch, H., & Martí-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 803. (4) Payne, H. M., & Hackney, R. L., Jr.: *ibid.*, p. 821. (5) McCrumb, F. R., Jr.; Snyder, M. J., & Hicken, W. J.: *ibid.*, p. 837.

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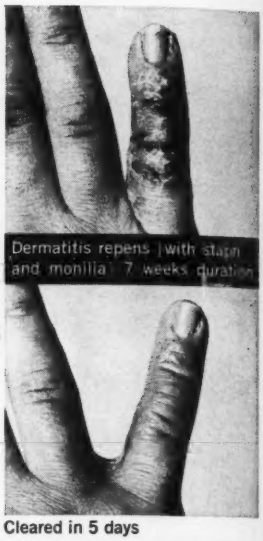

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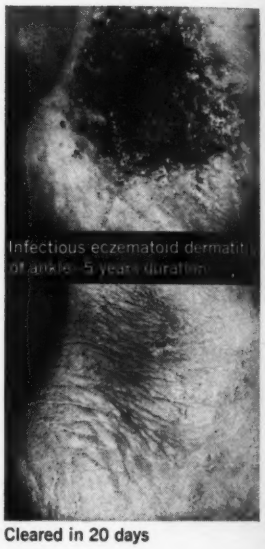

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References: 1. Shelmire, J.B., Jr.: Monographs on Therapy 3:164 (Nov.) 1958. • 2. Nix, T.E., Jr., and Derbes, V.J.: Monographs on Therapy 3:123 (Nov.) 1958. • 3. Robinson, R.C.V.: Bull. School of Med., U. Maryland 43:54 (July) 1958. • 4. Sternberg, T.H.: Newcomer, V.D., and Reisner, R.M.: Monographs on Therapy 3:115 (Nov.) 1958. • 5. Clark, R.F., and Hallett, J.J.: Monographs on Therapy, 3:153 (Nov.) 1958. • 6. Smith J.G., Jr.; Zawisza, R.J., and Blank, H.: Monographs on Therapy, 3:111 (Nov.) 1958. • 7. Monographs on Therapy, 3:137 (Nov.) 1958. • 8. Howell, C.M., Jr.: North Carolina M.J. 19:449 (Oct.) 1958. • 9. Bereston, E.S.: South. M.J. 50:547 (April) 1957.

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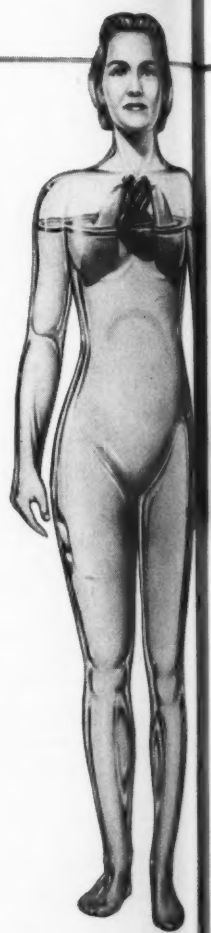

indications: Hypertension, congestive heart failure of all degrees of severity, premenstrual syndrome (edema), edema and toxemia of pregnancy, renal edema—nephrosis, nephritis; cirrhosis with ascites, drug-induced edema, and as adjunctive therapy in the management of obesity complicated by edema.

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bibliography: 1. Esch, A. F., Wilson, I. M. and Freis, E. D.: 3,4-Dihydrochlorothiazide: Clinical Evaluation of a New Saluretic Agent, Preliminary Report; M. Ann. District of Columbia **28**:9, (Jan.) 1959. 2. Ford, R. V.: The Clinical Pharmacology of Hydrochlorothiazide; Southern Med. J. **52**:40, (Jan.) 1959. 3. Fuchs, M., Bodi, T., Irie, S. and Moyer, J. H.: Preliminary Evaluation of Hydrochlorothiazide ('HYDRODIURIL'); M. Rec. & Ann. **51**:872, (Dec.) 1958. 4. Moyer, J. H., Fuchs, M., Irie, S. and Bodi, T.: Some Observations on the Pharmacology of Hydrochlorothiazide; Am. J. Cardiol. **3**:113, (Jan.) 1959.

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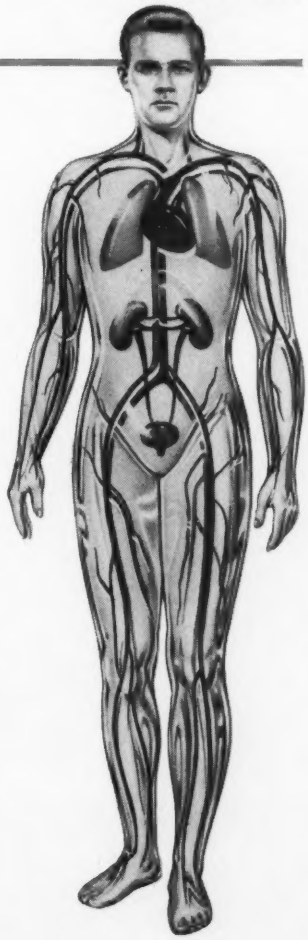
- provides background therapy to improve and simplify the management of all grades of hypertension
- has been reported by some investigators to have a greater antihypertensive effect in some patients than chlorothiazide at equivalent dosage
- does not lower blood pressure in normotensives
- reduces dosage requirements for other antihypertensive agents, often with concomitant reduction in their distressing side effects
- smooths out blood pressure fluctuations



precautions: It is important that the dosage be adjusted as frequently as the needs of the individual patient demand. When HYDRODIURIL is used with a ganglion blocking agent, it is mandatory to reduce the dose of the latter by at least 50 per cent, immediately upon adding HYDRODIURIL to the regimen.

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Clinical data ▶

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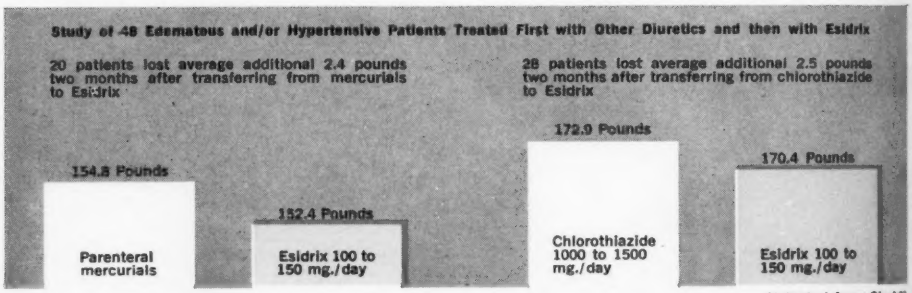
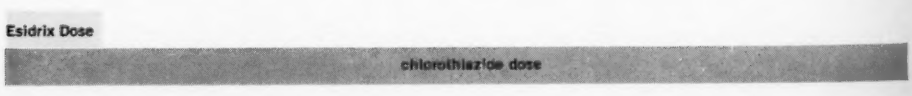
Esidrix relieves edema in many patients refractory to other diuretics: Studies reveal that certain patients unresponsive or refractory to mercurials and chlorothiazide respond readily to Esidrix. Brest and Likoff[1] observed that 9 of 12 patients with congestive heart failure—who failed to respond to other diuretics—were completely controlled with Esidrix. Esidrix appears to have clinical value even after the patient has developed partial tolerance to chlorothiazide, and may be found useful in cases of sensitivity to chlorothiazide.[2]

Therapy with Esidrix often results in more weight loss than with other diuretics: In a study[3] of 48 patients with edema and/or hypertension, who were treated originally with chlorothiazide or with mercurial diuretics, substitution of Esidrix at a dose of 100 to 150 mg./day resulted in additional average weight loss of 2.4 to 2.5 pounds.


Study of 48 Edematous and/or Hypertensive Patients Treated First with Other Diuretics and then with Esidrix
20 patients lost average additional 2.4 pounds two months after transferring from mercurials to Esidrix
28 patients lost average additional 2.5 pounds two months after transferring from chlorothiazide to Esidrix
154.8 Pounds
152.4 Pounds
172.9 Pounds
170.4 Pounds
Parenteral mercurials
Esidrix 100 to 150 mg./day
Chlorothiazide 1000 to 1500 mg./day
Esidrix 100 to 150 mg./day

(Adapted from Clark[3])



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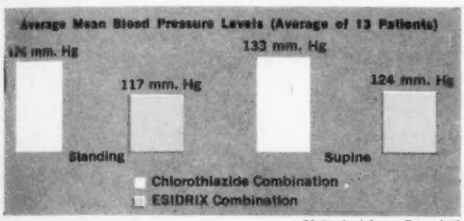
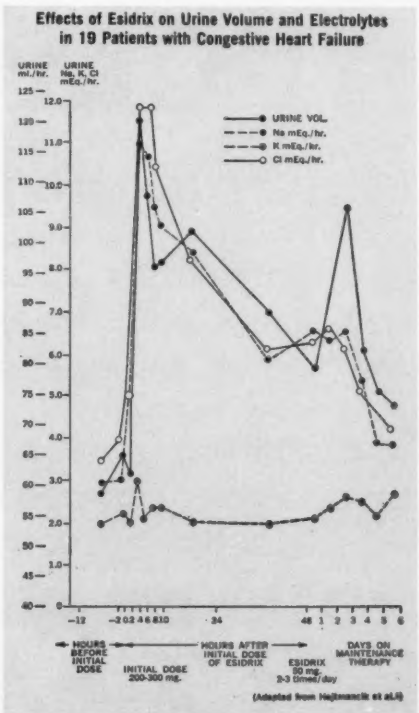
(hydrochlorothiazide CIBA)

Produces greater average reduction in blood pressure: Eleven of 13 hypertensive patients[4] were treated initially with a chlorothiazide-mecamylamine-reserpine combination (10 patients had 1000 mg. and 1 patient 500 mg. chlorothiazide daily); 1 patient had been treated with hydralazine and 1 had no previous medication. Nine were then transferred to an Esidrix-mecamylamine-reserpine combination and 4 to an Esidrix-reserpine combination for periods of 3 to 7 weeks (12 patients had 100 mg. and 1 patient 50 mg. Esidrix daily). Average mean blood pressure levels were recorded in the standing and supine positions. As shown in graph below, left, there was a further drop in blood pressure after patients were transferred to Esidrix.



[Adapted from Dennis[4]]

Exceptional safety... reduced likelihood of electrolyte imbalance: While Esidrix markedly increases sodium and chloride excretion, it has far less effect on excretion of potassium (see chart at right) and bicarbonate. Hence, there is little likelihood of disturbing electrolyte balance when recommended procedures are followed.


Effects of Esidrix on Urine Volume and Electrolytes in 19 Patients with Congestive Heart Failure
URINE ml./hr.
URINE Na, K, Cl mEq./hr.
URINE VOL.
Na mEq./hr.
K mEq./hr.
Cl mEq./hr.
HOURS BEFORE INITIAL DOSE
INITIAL DOSE 200-300 mg.
HOURS AFTER INITIAL DOSE OF ESIDRIX
ESIDRIX 50 mg. 2-3 times/day
DAYS ON MAINTENANCE THERAPY

DOSAGE: Esidrix is administered orally in an average dose of 75 to 100 mg. daily, with a range of 25 to 200 mg. A single dose may be given in the morning or tablets may be administered 2 or 3 times a day.

SUPPLIED: *Tablets,* 25 mg. (pink, scored); bottles of 100 and 1000. *Tablets,* 50 mg. (yellow, scored); bottles of 100 and 1000.

Al-Caroid®

controls the double trouble...

1. hyperacidity relieved – In AL-CAROID, selected antacids act promptly to relieve heartburn, flatulence and other distressing symptoms of gastric hyperacidity.

2. digestion maintained – AL-CAROID contains the proteolytic enzyme – Caroid® – which is not inactivated by antacids, thus assuring maintenance of protein digestion.

Powder/Tablets *Write for samples*

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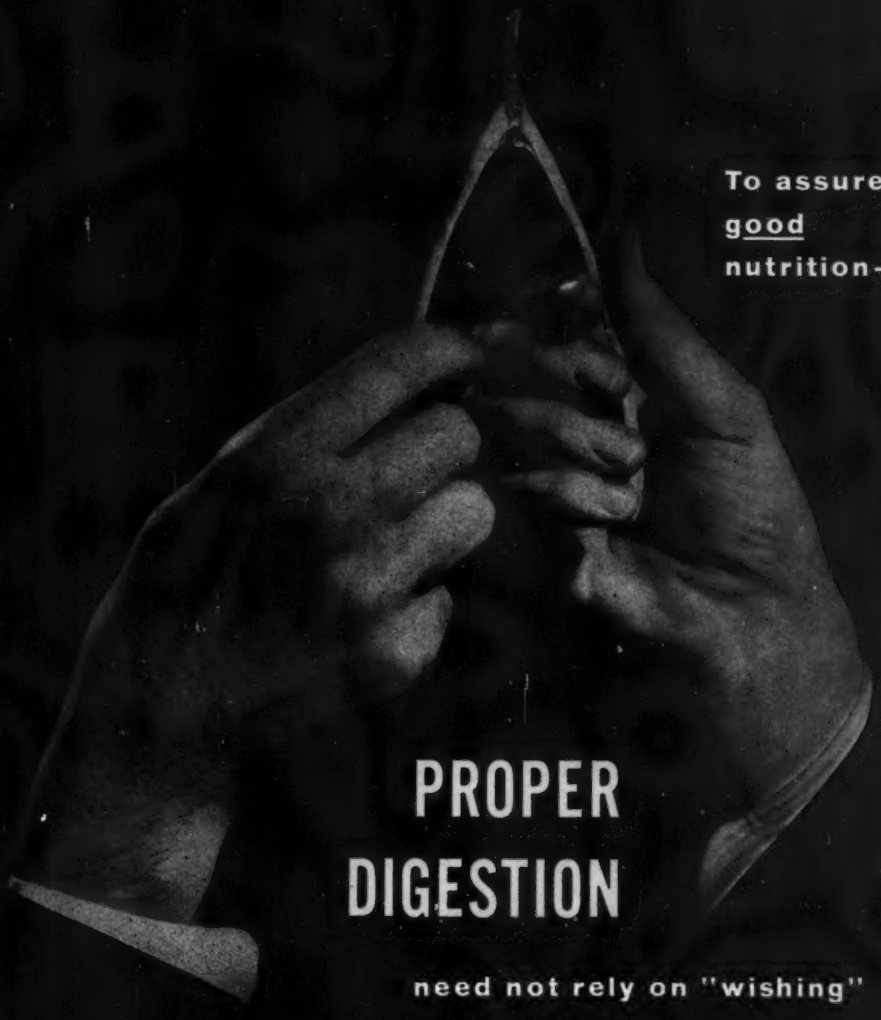


To assure
good
nutrition—

PROPER DIGESTION

need not rely on "wishing"

Each double layered Entozyme tablet contains:

Pepsin, N.F. 250 mg.
—released in the stomach from gastric soluble outer coating of tablet.

Pancreatin, U.S.P. 300 mg.

Bile Salts 150 mg.
—released in the small intestine from enteric coated inner core.

A. H. ROBINS CO., INC.
Richmond 20, Virginia
Ethical Pharmaceuticals of Merit since 1878

As a comprehensive supplement to deficient natural secretion of digestive enzymes, particularly in older patients, ENTOZYME effectively improves nutrition by bridging the gap between adequate ingestion and proper digestion. Among patients of all ages, it has proved helpful in chronic cholecystitis, post-cholecystectomy syndrome, subtotal gastrectomy, pancreatitis, dyspepsia, food intolerance, flatulence, nausea and chronic nutritional disturbances.

For comprehensive digestive enzyme replacement—

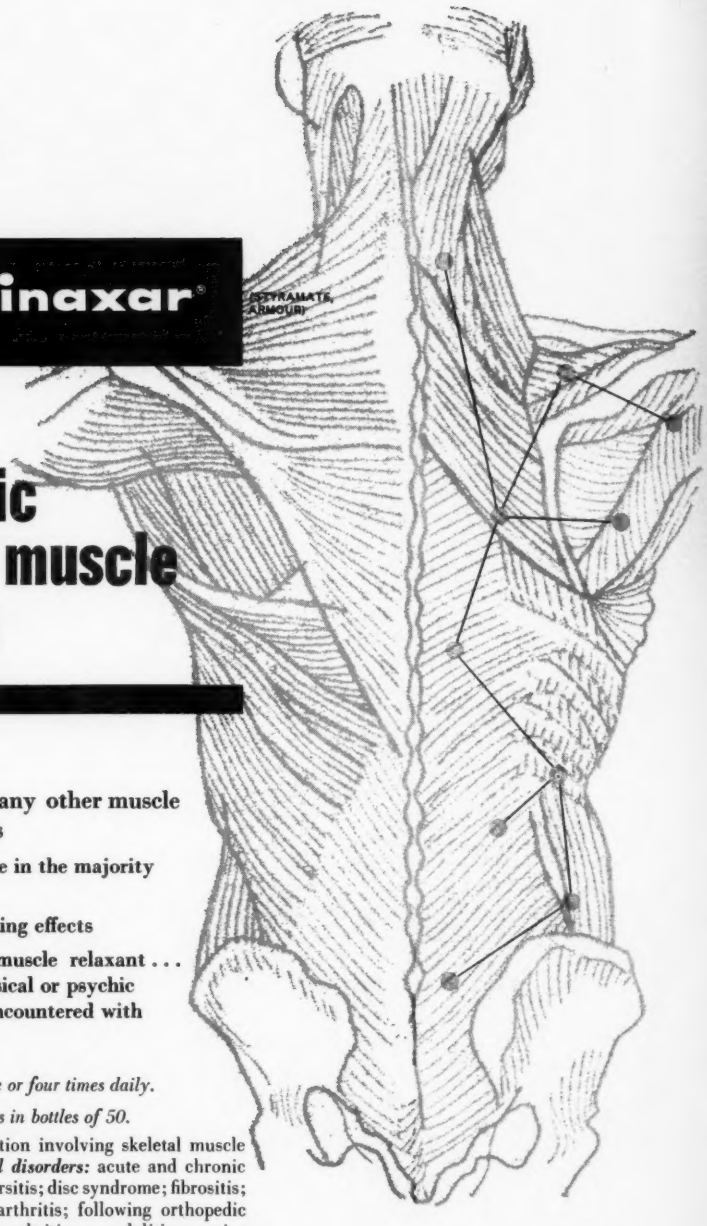
ENTOZYME

Robins

rely on

Sinaxar® (ESTYRAMATE, ARMOUR)

a specific skeletal muscle relaxant



Chemically unlike any other muscle relaxant, Sinaxar is

- **consistently effective in the majority of cases**
- **long acting: no fleeting effects**
- **purely a skeletal muscle relaxant . . . free of adverse physical or psychic effects frequently encountered with tranquilizers**

DOSAGE: *Two tablets three or four times daily.*

SUPPLIED: *200 mg. tablets in bottles of 50.*

INDICATIONS: Any condition involving skeletal muscle spasm, as ***musculoskeletal disorders:*** acute and chronic back ache; arthritides; bursitis; disc syndrome; fibrositis; myalgia; myositis; osteoarthritis; following orthopedic procedures; rheumatoid arthritis; spondylitis; sprains and strains; torticollis; ***neurologic disorders:*** cerebral palsy; cerebrovascular accidents; cervical root syndrome: multiple sclerosis.

ARMOUR

ARMOUR PHARMACEUTICAL COMPANY • *A Leader in Biochemical Research* • KANKAKEE, ILLINOIS

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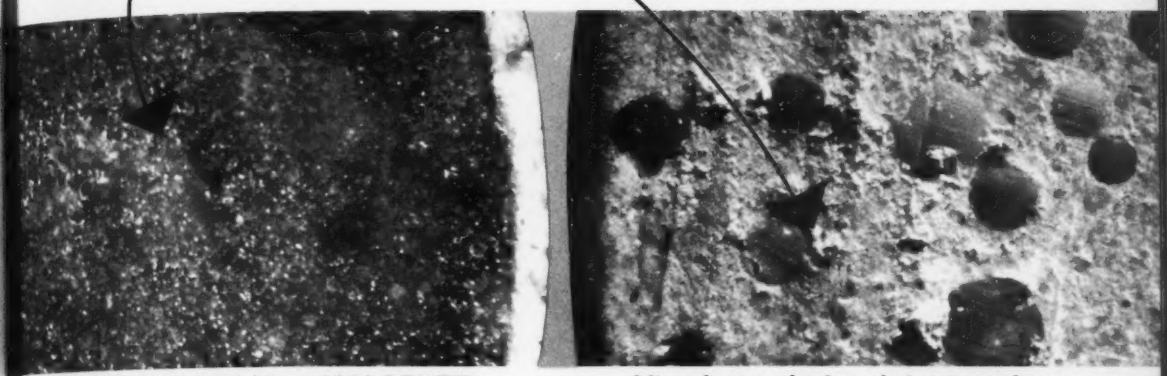

Microphotograph of a **HOMAGENET**

Microphotograph of usual vitamin product

The photographs above point out the difference between Homagenets and many vitamin products. By means of the homogenization process, both oil and water soluble vitamins are presented in microscopic particles. Due to the fine particle size, there is much greater surface exposure, which permits quicker absorption and better utilization. This has been clinically proved by Lewis and others.[1]

1. Lewis, J.M., et al.: J. Pediatrics, *31*:496

HOMAGENETS®

The only homogenized vitamins in solid form

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Here
are the advantages
of

HOMAGENETS®*

the only
homogenized vitamins
in solid form

The advantages of HOMAGENETS

- Pleasant, candy-like flavor
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- Excess vitamin dosage unnecessary
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- No "fishy burp"
- May be chewed, swallowed or dissolved in the mouth.

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PRENATAL—Contains iron and calcium as a dietary supplement during gestation.

GERIATRIC—A complete formula for the prevention of vitamin-mineral deficiencies.

AORAL—Useful in the treatment of certain types of skin disorders.

THERAPEUTIC—Particularly indicated during convalescence and stress periods.

*U.S. Pat. 2676136. Other Pat. Pending

Currently, mailings will be forwarded only at your request. Write for samples and literature.

THE S.E. MASSENGILL COMPANY Bristol, Tennessee · New York · Kansas City · San Francisco

"I seem to have the blues all the time... I can't sleep..."

in the depressed, unhappy patient

PROMPTLY IMPROVES MOOD

without excitation

- **Acts fast to relieve depression and its common symptoms:** sadness, crying, anorexia, listlessness, irritability, rumination, and insomnia.
- **Restores normal sleep**—without hang-over or depressive aftereffects. Usually eliminates need for sedative-hypnotics.

EFFICACY AND SAFETY CONFIRMED IN OVER 3,000 DOCUMENTED CASE HISTORIES.[1,2,3]

Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this dose may be gradually increased up to 3 tablets q.i.d.

Composition: Each light-pink, scored tablet contains 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.

References:

1. Alexander, L.: J.A.M.A. 166:1019, March 1, 1958.
2. Current personal communications; in the files of Wallace Laboratories.
3. Pennington, V.M.: Am. J. Psychiat. 115:250, Sept. 1958.

▲Deprol▲†

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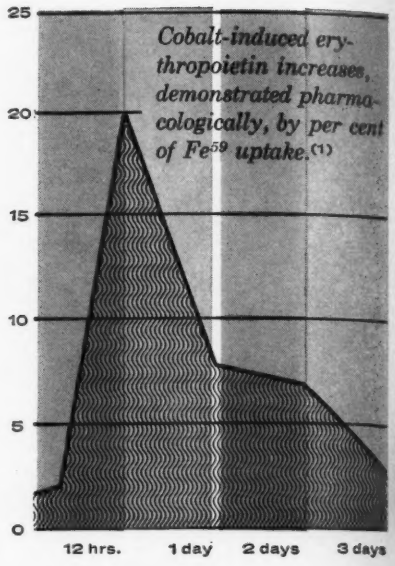

Cobalt-induced erythropoietin increases, demonstrated pharmacologically, by per cent of Fe^{59} uptake.(1)

Activates the physiologic mechanism in anemia therapy

RONCOVITE®-mf

Each tablet contains: Cobalt chloride (Cobalt as Co..3.7 mg.)..15 mg., Ferrous Sulfate, exsiccated..100 mg.

Only cobalt among therapeutic agents enhances production of erythropoietin to promote red cell formation.[1,2,3]

With Roncovite-MF, increased erythropoietin production permits excellent hematopoietic response with sharply reduced iron dosage.

Cobalt-iron (Roncovite therapy) has been demonstrated as superior to iron alone in the common hypochromic anemias such as menstrual anemia, anemia of pregnancy, nutritional anemia of infancy and refractory anemias of chronic infection.[4,5,6,7,8]

(1) Goldwasser, E.; Jacobson, L. O.; Fried, W., and Pizak, L. F.: Blood 13:55 (Jan.) 1958. (2) Gurney, C. W.; Jacobson, L. O. and Goldwasser, E.: Ann. Int. Med. 49:363 (Aug.) 1958. (3) Korst, D. R.; Bishop, R. C. and Bethell, F. H.: J. Lab. & Clin. Med. 52:364 (Sept.) 1958. (4) Ausman, D. C.: Journal-Lancet 76:290 (Oct.) 1956. (5) Holly, R. G.: Obst. & Gynec. 9:299 (Mar.) 1957. (6) Holly, R. G.: Clin. Obst. & Gynec. 1:15 (Mar.) 1958. (7) Diamond, E. F.; Gonzales, F., and Pisani, A.: Illinois M. J. 113:154 (April) 1958. (8) Hill, J. M.; La Jous, J., and Sebastian, F. J.: Texas State J. Med. 51:686 (Oct.) 1955.

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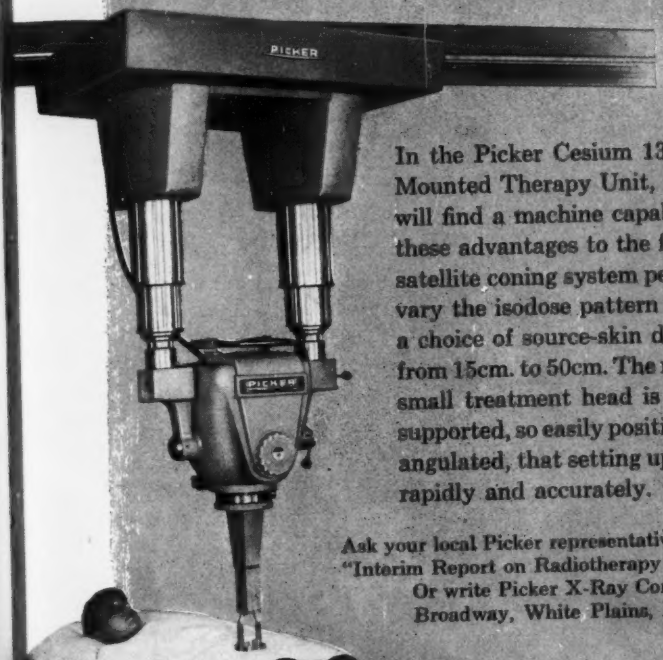
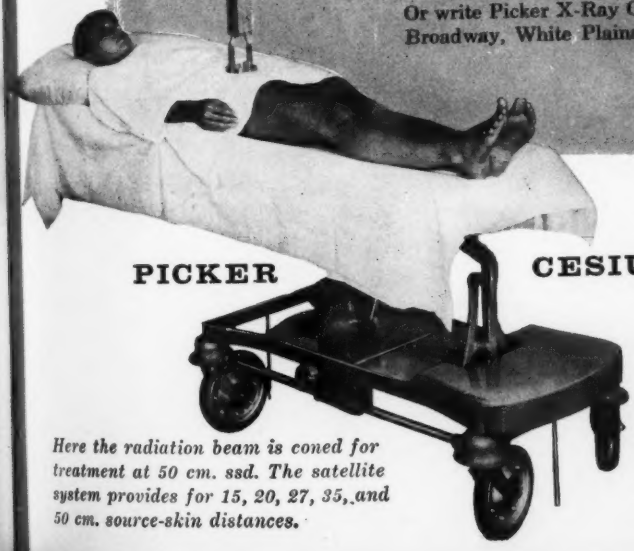
"Snap-On" cones are held in a strong magnetic grip, are easily attached or detached. Once in place, they can be rotated within the holding ring as required. Here the 15 cm. ssd cone is being attached.

The prospective abundant availability of Cesium 137 has fired the imagination of radiotherapists to a lively degree. Compared to Cobalt 60, its longer half life, its lower cost, its lesser shielding, its smaller treatment head, and its therapeutic versatility hold great promise.



In the Picker Cesium 137 Ceiling Mounted Therapy Unit, the therapist will find a machine capable of exploiting these advantages to the full. Its satellite coning system permits him to vary the isodose pattern by treating at a choice of source-skin distances ranging from 15cm. to 50cm. The relatively small treatment head is so flexibly supported, so easily positioned and angulated, that setting up the case goes rapidly and accurately.

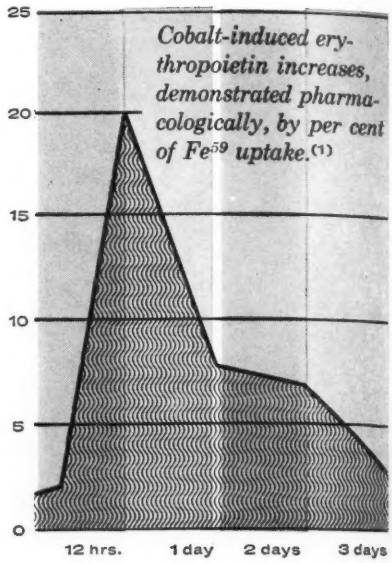
Ask your local Picker representative for a copy of our "Interim Report on Radiotherapy with Cesium 137". Or write Picker X-Ray Corporation, 25 South Broadway, White Plains, New York.



PICKER **CESIUM[137] THERAPY UNIT**

Here the radiation beam is coned for treatment at 50 cm. ssd. The satellite system provides for 15, 20, 27, 35, and 50 cm. source-skin distances.

x-ray



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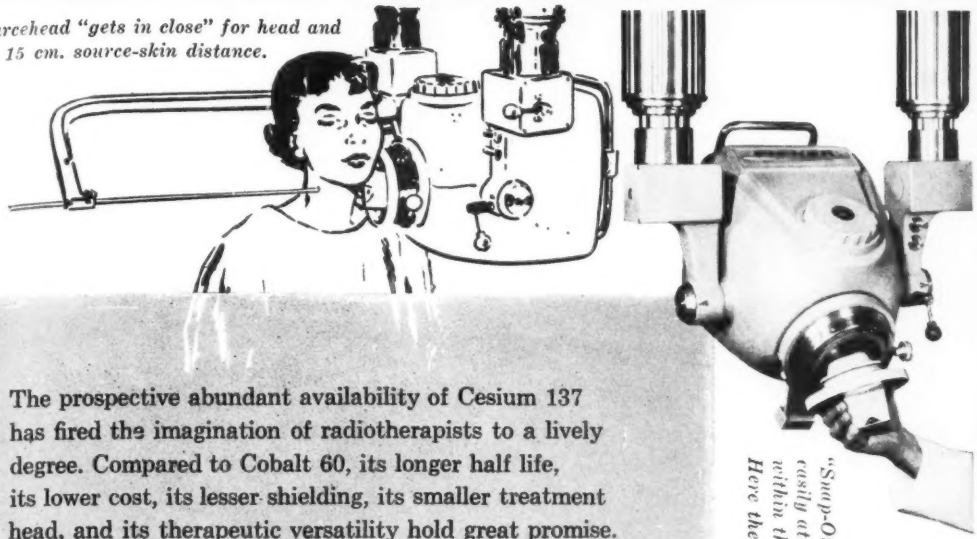

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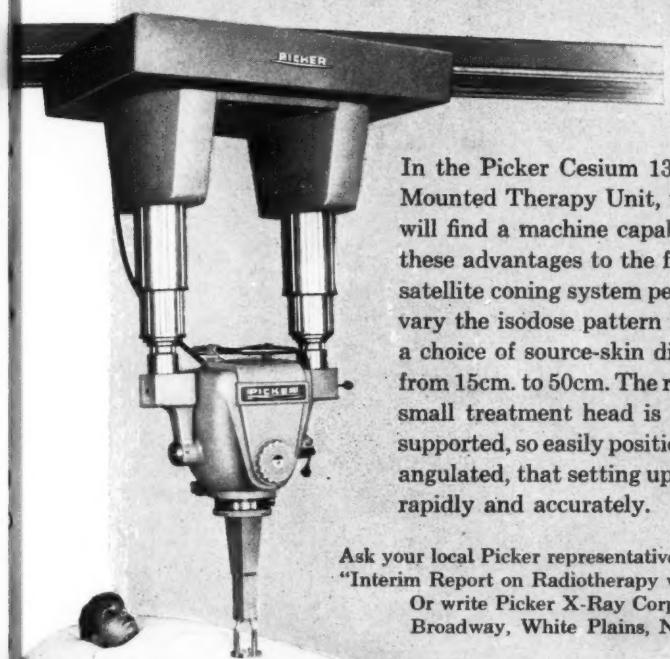

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0.2 Gram (or 3 grains)
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Nasal patency in minutes for hours

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SUPERIOR NASAL DECONGESTANT

Nasal Solution, 1-oz. dropper bottle and pint bottle, 0.1%. ***Nasal Spray,*** 15 cc., in plastic bottle, 0.1%.
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Note: As with certain other widely used nasal decongestants, overdosage may cause drowsiness or deep sleep in infants and young children: KEEP OUT OF REACH OF CHILDREN OF ALL AGES. The Pediatric Nasal Drops (0.05%) for children under 6 yrs. and Tyzine Nasal Spray is administered, it should be held only in an upright position.

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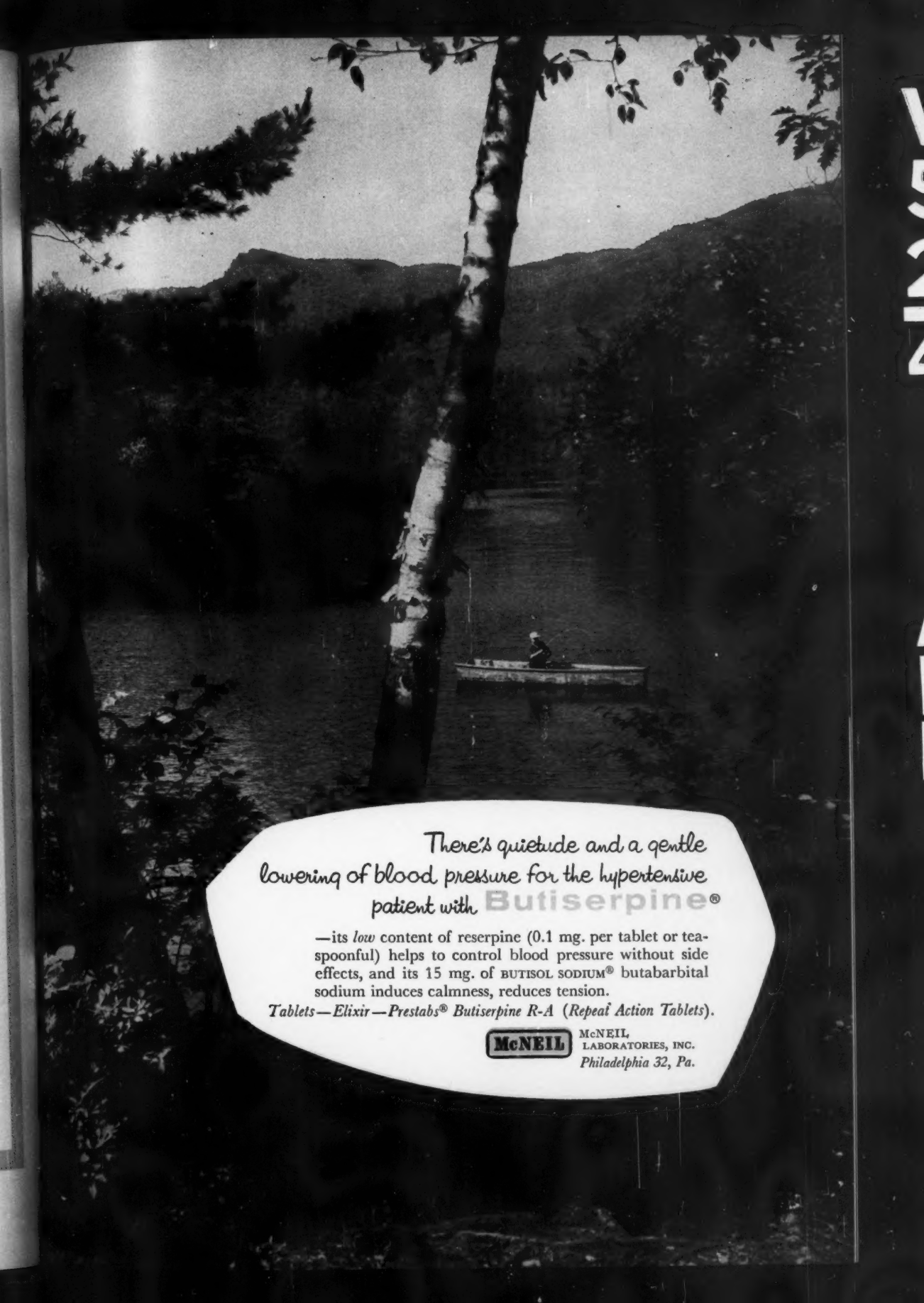
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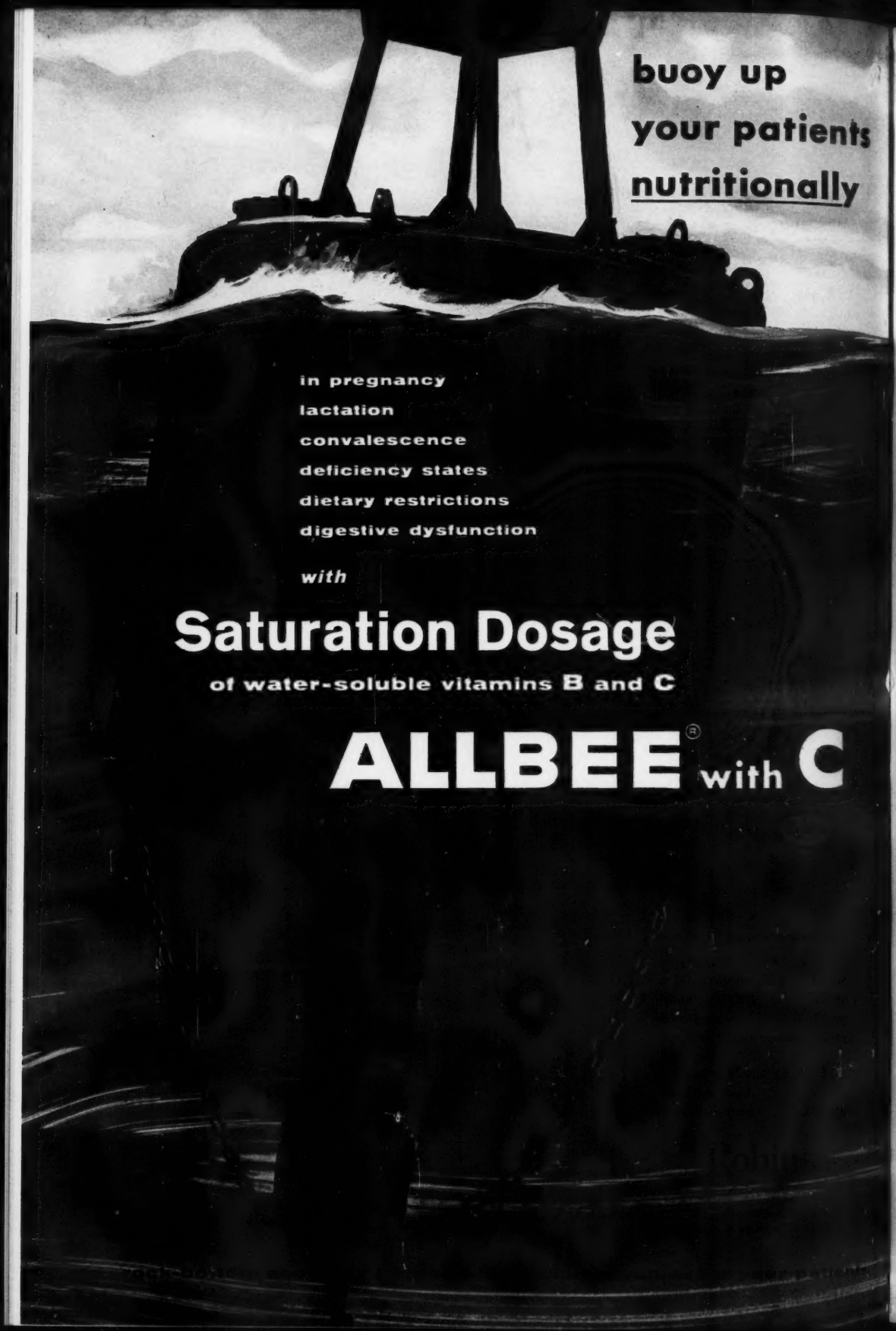
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AND FOR RELIEF OF MODERATE TO SEVERE VISCERAL, NEURAL AND SOMATIC PAIN

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DOSAGE: Adult dose is 1 to 2 tablets orally, repeated if necessary every 3 or 4 hours.

Tablets containing Demerol hydrochloride 50 mg., acetyl-p-aminophenol 300 mg., bottles of 100.

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Triple action of Demerol,® APAP and dihydrocodeinone for:

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Cough suppressant action of dihydrocodeinone—at least six times as potent as codeine but essentially nonconstipating—enhanced by the broncho-spasmolytic effects of Demerol.

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Addition of Demerol to APAP and dihydrocodeinone provides more complete relief of mild to moderate pain. The mild sedation without respiratory depression is widely beneficial.

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APAP—Active metabolite of phenacetin—produces more rapid and prolonged fever reduction than aspirin or APC without gastric irritation or hematologic changes.

AVAILABILITY: stratified green, white and pink tablets containing Demerol hydrochloride 25.0 mg., dihydrocodeinone bitartrate 5.0 mg., acetyl-p-aminophenol 150 mg., bottles of 100.

DOSAGE: one or two tablets

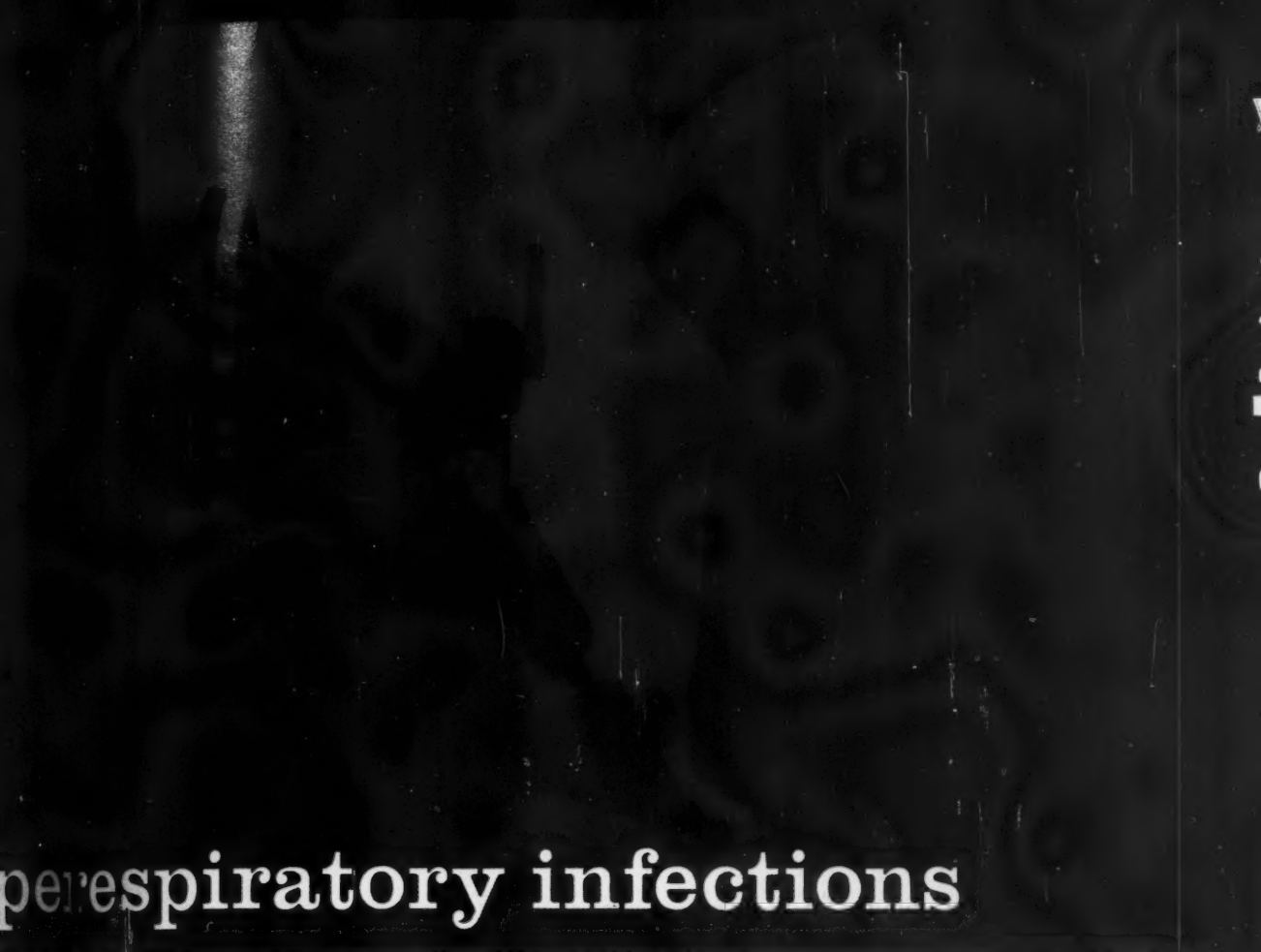
now...when treating upper

Madribon

Disease	No. of Patients	Response: Good or Excellent	Pe
Otitis media	72	65	
Bronchitis	11	10	
Obstructive laryngotracheitis	3	3	
Tonsillitis	21	18	
Cervical adenitis	13	13	
Purulent rhinitis or sinusitis	19	16	
Total	139	125	

From a study by E. H. Townsend and A. Borgstedt[1]

safe "No side reactions to sulfadimethoxine were observed in the en series of 167 patients."[1] **effective** "Remarkable improvement, charac ized by subjective relief and disappearance of inflammatory symptoms, curred in 107 out of the 111 patients under study."[2] **economical** addition to the clinical efficiency attributable to sulfadimethoxine... the ec omy involved in medication with a fast-acting chemotherapeutic agent w rants its early use...."[3]



ne fastest growing antibacterial bibliography:

H. Townsend and A. Borgstedt, *Antibiotics Annual 1958-*, in press. **2.** J. C. Elia, *Antibiotic Med. & Clin. Therapy*, *6*:ppl. 1), 1959. **3.** B. H. Leming, Jr., C. Flanigan, Jr. and B. R. nings, *Antibiotic Med. & Clin. Therapy*, *6*:(Suppl. 1), 1959. I. P. Ironson and C. Patel, *Antibiotic Med. & Clin. Therapy*, *6*:ppl. 1), 1959. **5.** S. Ross, J. R. Puig and E. A. Zaremba, *Anti-ics Annual 1958-1959*, in press. **6.** J. D. Young, Jr., W. S. Kiser 0. C. Beyer, *Antibiotic Med. & Clin. Therapy*, *6*:(Suppl. 1), 9. **7.** T. D. Michael, *Antibiotic Med. & Clin. Therapy*, *6*:ppl. 1), 1959. **8.** W. A. Leff, *Antibiotic Med. & Clin. Therapy*, Suppl. 1), 1959. **9.** B. A. Koechlin, W. Kern and R. Engelberg, *tibiotic Med. & Clin. Therapy*, *6*:(Suppl. 1), 1959. **10.** R. J. Schnitzer and W. F. DeLorenzo, *Antibiotic Med. & Clin. Therapy*, *6*:(Suppl. 1), 1959. **11.** R. J. Schnitzer, W. F. DeLorenzo, E. Grunberg and R. Russomanno, *Proc. Soc. Exper. Biol. & Med.*, *99*:421, 1958. **12.** W. F. DeLorenzo and R. Russomanno, *Antibiotic Med. & Clin. Therapy*, *6*:(Suppl. 1), 1959. **13.** B. Fust and E. Boehni, *Antibiotic Med. & Clin. Therapy*, *6*:(Suppl. 1), 1959. **14.** W. F. DeLorenzo and A. M. Schumacher, *Antibiotic Med. & Clin. Therapy*, *6*:(Suppl. 1), 1959. **15.** W. P. Boger, *Antibiotics Annual 1958-1959*, in press. **16.** O. Brandman, C. Oyer and R. Engelberg, *J. M. Soc. New Jersey*, *56*:24, Jan. 1959. **17.** J. F. Glenn, J. R. Johnson and J. H. Semans, *Antibiotic Med. & Clin. Therapy*, *6*:(Suppl. 1), 1959.

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Physicians in Indianapolis explain why they prescribe Serpasil® for hypertension

Physicians in Indianapolis, as all over the world, realize that Serpasil has two special advantages for many hypertensive patients:

1. The Central Effect: Serpasil calms those who are anxious or tense as well as hypertensive.

2. The Bradycrotic Effect: The heart-slowing effect of Serpasil relieves the tachycardia that so often accompanies high blood pressure.

These facts about Serpasil were found in reports from 450 physicians in the U.S. (part of a world-wide survey*): 74 per cent of *hyperanxious hypertensives* treated with Serpasil showed excellent or good over-all response; 80 per cent of patients with *tachycardia* showed excellent or good response.

When marked anxiety-tension or tachycardia are part of the hypertensive picture, Serpasil can help your patient in more ways than one.

DOSAGE: Average initial daily dose, 0.5 mg. with a range of 0.1 to 1 mg. Reduce in one week to 0.25 mg. or less daily for maintenance.

SUPPLIED: *Tablets*, 0.1 mg., 0.25 mg., 1 mg., 2 mg., and 4 mg. *Elixirs*, 0.2 mg. and 1 mg. per 4-ml. teaspoon. *Samples available on request.*

*Complete information from this survey will be sent on request. SERPASIL® (reserpine CIBA)

CIBA

2/2643 MB

Four weeks ago, Mrs. C. was an anxiety patient, complaining of weakness, trembling, sweating, tachycardia, on the slightest exertion. Her symptoms followed family reverses; home life became disorganized, she couldn't cope with housework. Therapy with TRILAFON, 4 mg. t.i.d., and a weekly office visit to discuss her feelings have worked wonders in reactivating this patient. She's on maintenance dosage now, 2 mg. t.i.d., able to work very well, and wide-awake and active all day long.

mobilizes patients immobilized by anxiety

Trilafon®
perphenazine

when you want to avoid drowsiness

- helps the patient contain anxiety, tension
- restores normal working capacity

TRILAFON Tablets—2 mg. and 4 mg.; bottles of 50 and 500.
TRILAFON REPETABS,® 8 mg.—4 mg. for *prompt* effect in the outer layer and 4 mg. for *prolonged relief* in the timed-action inner core; bottles of 30 and 100.
For complete details on TRILAFON consult Schering literature.

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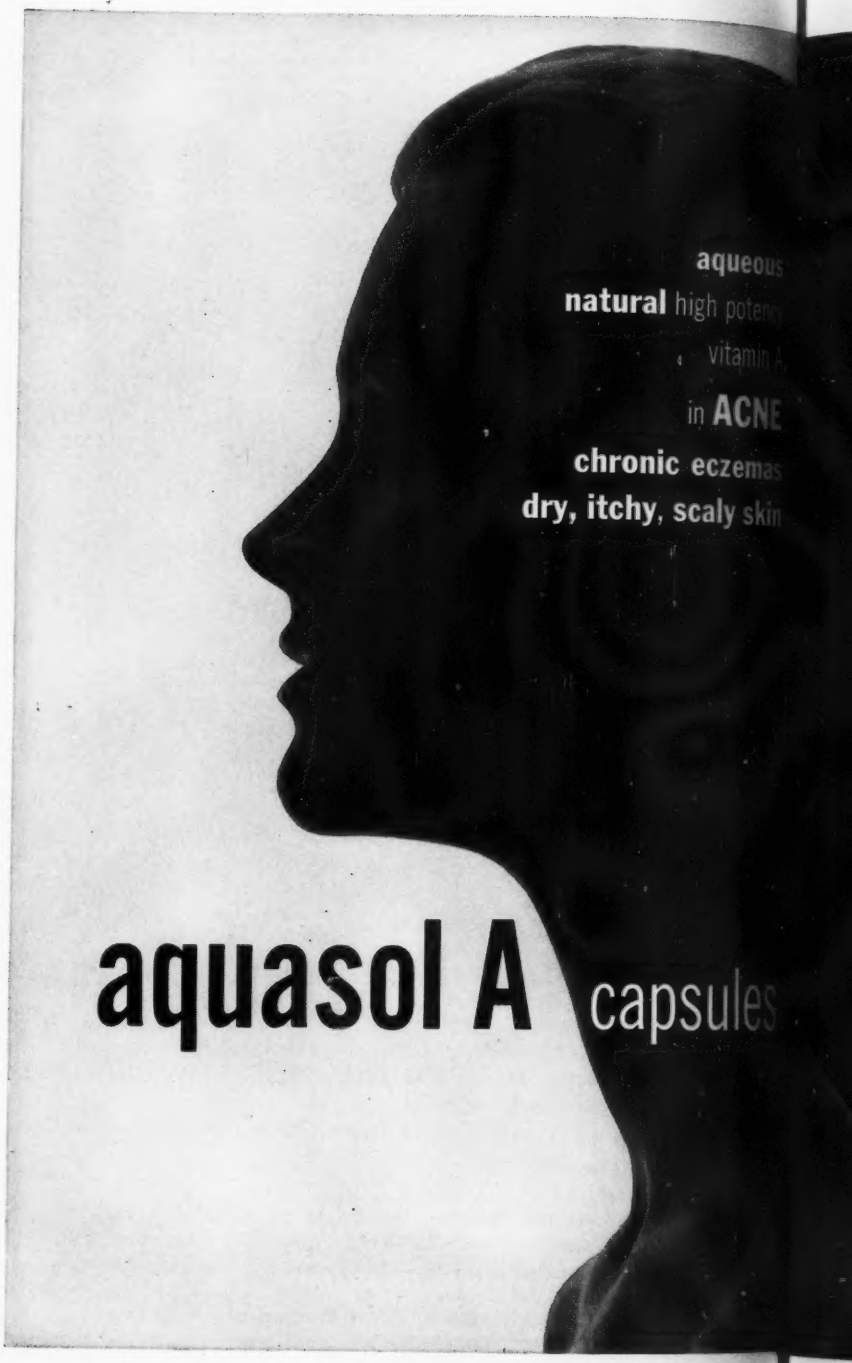
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more readily, rapidly, completely reaches the affected tissues because there is

"greater diffusibility of vitamin A from aqueous dispersion into the tissues."[1]

aquasol A capsules — the most widely used of all oral vitamin A products, for these good reasons . . .

aqueous vitamin A is more promptly, more fully, more dependably absorbed and utilized.

natural vitamin A is more effective because it is directly utilized physiologically.

well tolerated — fish taste, odor and allergens are removed by special processing.

economical — less dosage is needed and treatment time is sharply reduced as compared to oily vitamin A.

three separate high potencies of (water-solubilized natural vitamin A) per capsule:

25,000 U.S.P. units
50,000 U.S.P. units
100,000 U.S.P. units

bottles of 100, 500 and 1000 capsules

Samples and literature available upon request.

u. s. vitamin & pharmaceutical
CORPORATION
(Arlington-Funk Laboratories, division)
250 East 43rd Street • New York 17, N. Y.

1. Davidson, D. D. and Sobel, A. E.: J. Invest. Derm. 12 221, 1949

AN AMES CLINIQUICK™

CLINICAL BRIEFS FOR MODERN PRACTICE

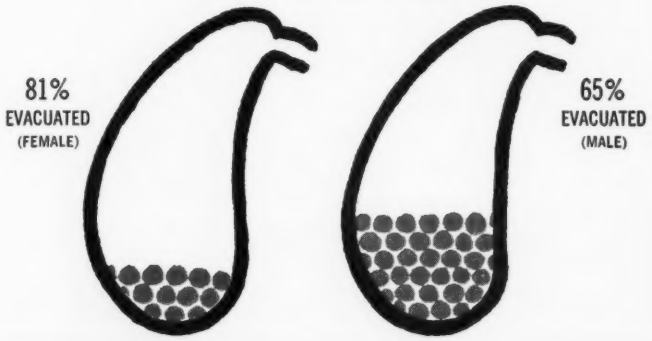
how do age and sex influence evacuation of the gallbladder?

Children and pre-adolescents, especially boys, have a faster emptying rate than adults. After puberty, the gallbladder of the male is slower in emptying—elderly women have a faster gallbladder evacuation rate than elderly men.

**Source:* Lichtman, S. S.: Diseases of the Liver, Gallbladder and Bile Ducts, ed. 3, Philadelphia, Lea & Febiger, 1953, vol. 2, p. 1178.

GALLBLADDER EVACUATION IN THE ELDERLY*

30 minutes after meal of egg yolk



true hydrocholeresis plus reliable spasmolysis...

DECHOLIN® with Belladonna

- relieves the pain of smooth-muscle spasm
- steadies the "nervous gut"
- facilitates biliary and pancreatic drainage

available: DECHOLIN with Belladonna Tablets: dehydrocholic acid, AMES 3¾ gr. (250 mg.) and extract of belladonna ⅙ gr. (10 mg.). Bottles of 100 and 500.

for free-flowing "therapeutic bile"...

DECHOLIN®

(dehydrocholic acid, AMES)

- medical and postoperative management of biliary tract disorders
- routine physiologic support for geriatric patients
- constipation—natural physiologic laxation without catharsis

available: DECHOLIN Tablets: dehydrocholic acid, AMES 3¾ gr. (250 mg.). Bottles of 100, 500 and 1000; drums of 5000.

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Elkhart • Indiana
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Still in the picture *with...*

NIATRIC™

TABLETS AND ELIXIR

To add life to years—not merely years to life . . . Niatric sharpens mental acuity and promotes a return to more normal social and physical activity for your aged patients.

In the Old Age Syndrome . . . Niatric relieves confusion, forgetfulness, irritability, depression and apathy—the penalties of advancing age.

- **Niatric improves respiration and cerebral function**
- **Niatric improves circulation**
- **Niatric protects capillary integrity**
- **Niatric prevents brain tissue hypoxia**

Niatric contains:	Each Tablet:	5 cc. Elixir:
Pentylenetetrazol	100 mg.	100 mg.
Nicotinic Acid	50 mg.	50 mg.
Ascorbic Acid	100 mg.	100 mg.
Bioflavonoids	100 mg.	-----
Alcohol	-----	15%

Average Dose: 1 tablet or 1 tsp. (5 cc.) t.i.d.
Supply: Tablets, bottles of 100 and 500.
Elixir, bottles of 1 pint.

Send now for samples and literature...

B. F. ASCHER AND COMPANY, INC.
Ethical Medicinals / Kansas City, Missouri

"EXCELLENT,"[3]

"MARKED,"[1]

"PRONOUNCED,"[2]

"SIGNIFICANT"[4] or

"GRATIFYING"[5]

results in 80.3% of cases of acute skeletal muscle spasm, and "moderate" results in 14.1%—or an over-all beneficial result in 94.4% of cases. Relatively free of adverse side effects.[1,2,4,5]

Now—in acute skeletal muscle spas

A SPEEDIER RETURN T

1 **In 33 adults with skeletal muscle spasm secondary to acute trauma:**

"All patients of this group received some degree of relief from the drug, and it is interesting that there was a significant degree of reduction in skeletal muscle spasm in 96% of these patients."[1]

2 **In 39 patients with herniated lumbar and cervical discs, who received methocarbamol for relief of pain and muscle spasm:**

"The response was judged to be pronounced in 25" . . . "moderate" in 13. "In most instances the attacks subsided quickly, so that the patients could continue to work or go back to work sooner than expected."[2]

3 **In 17 patients with acute muscle spasm:**

"An excellent result, after methocarbamol administration, was obtained in all patients with acute skeletal muscle spasm."[3]

4 **In 30 patients with pyramidal tract and acute myalgic disorders:**

"Use of this drug (Robaxin) resulted in significant improvement in 27 (90%), questionable improvement in 2, and none in 1 . . . No side-effects developed after 72 hours on the medication."[4]

5 **In 60 industrial workers with uncomplicated skeletal muscle spasm:**

"Results were gratifying in that 55 workers, or 92%, could return to full or light duty. No side effects were encountered."[5]

Supply: ROBAXIN Tablets, 0.5 Gm., in bottles of 50.

References: 1. Carpenter, E. B.: Southern M.J. 51:627, 1958. 2. Forsyth, H. F.: J.A.M.A. 167:163, 1958. 3. O'Doherty, D. S., and Shields, C. D.: J.A.M.A. 167:160, 1958. 4. Park, H. W.: J.A.M.A. 167:168, 1958. 5. Plumb, C. S.: Journal-Lancet 78:531, 1958.

A. H. ROBINS COMPANY, INC.
Richmond 20, Virginia
Ethical Pharmaceuticals of Merit since 1878

Robins

ORMAL ACTIVITY"
Beneficial results in 94.4% of patients in 5 clinical studies 1,2,3,4,5
Robaxin®
Methocarbamol Robins
U.S. Pat. No. 2770649

for dependable
relief of
smooth muscle spasm
VE4

Good reason, why DONNATAL – after 25 years of successful results – is prescribed *today* by more physicians than any other antispasmodic. DONNATAL provides effective "autonomic sedation," through *natural* belladonna alkaloids in optimal synergistic ratio, with phenobarbital.

4 BILLION DOSES

testify to the effectiveness and safety of Donnatal

DONNATAL® TABLETS, CAPSULES, ELIXIR

For everyday dosage flexibility

- For continuous antispasmodic action under a t.i.d. dosage regimen
- For occasional or temporary episodes of spasm
- For fluctuating dosage as required
- For relieving dosage monotony through 3-way variety

DONNATAL® EXTENTABS®

For all-day (or all-night) effects on a single dose

Provides the intensity of effect of *one* DONNATAL tablet, uniformly sustained for 10 to 12 hours:

- For continuous 24-hour relief on q. 12 h. dosage
- For eliminating up-and-down antispasmodic effects
- For assuring a full night's uninterrupted sleep
- For avoiding forgotten doses during a busy day

	In each Tablet, Capsule, or 5 cc. Elixir	In each Extentab
Hyoscyamine sulfate	0.1037 mg.	0.3111 mg.
Atropine sulfate	0.0194 mg.	0.0582 mg.
Hyoscine hydrobromide	0.0065 mg.	0.0195 mg.
Phenobarbital	(¼ gr.) 16.2 mg.	(¾ gr.) 48.6 mg.

DONNATAL®

A. H. ROBINS CO., INC., RICHMOND 20, VA.

Ethical Pharmaceuticals of Merit since 1878

Robins

If he needs nutritional support...

he deserves

GEVRAL®

Vitamin-Mineral Supplement Lederle

CAPSULES—14 VITAMINS—11 MINERALS

LEDERLE LABORATORIES, a Division of
AMERICAN CYANAMID COMPANY, Pearl River, New York

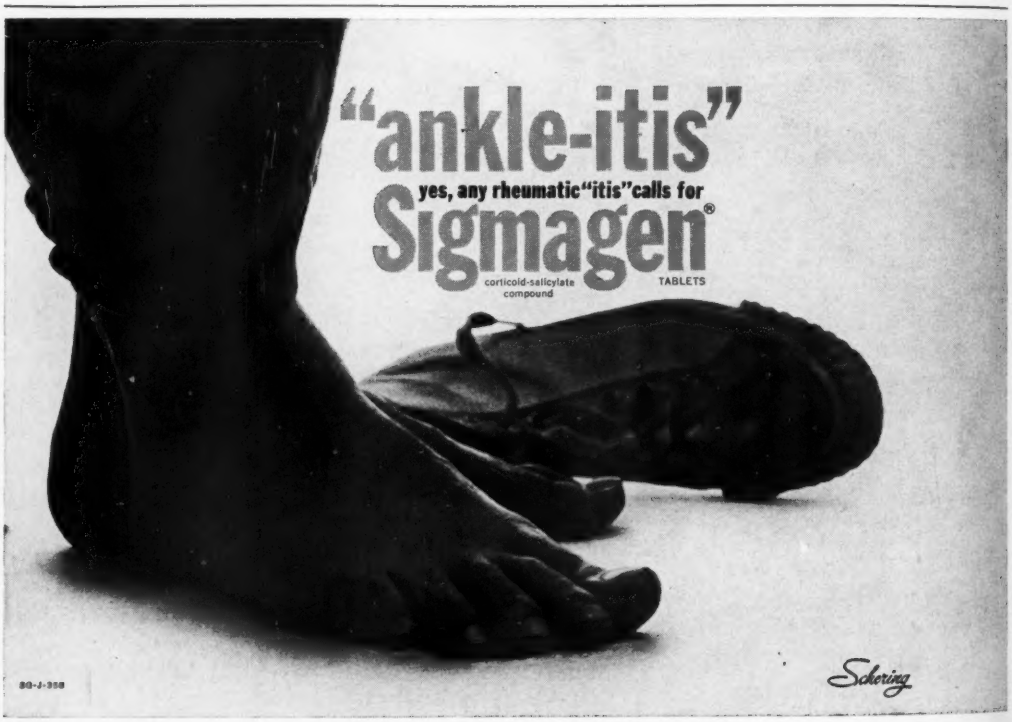
Lederle

"ankle-itis"

yes, any rheumatic "itis" calls for

Sigmagen®

corticoid-salicylate compound TABLETS



Schering

A workhorse "mycin" for common infections

respiratory infections

prompt, high blood levels

consistently reliable and reproducible blood levels

minimal adverse reactions

With well-tolerated CYCLAMYCIN, you will find it possible to control many common infections rapidly and to do so with remarkable freedom from untoward reactions. CYCLAMYCIN is indicated in numerous bacterial invasions of the respiratory system—lobar pneumonia, bronchopneumonia, tracheitis, bronchitis, and other acute infections. It has been proved effective against a wide range of organisms, such as pneumococci, H. influenzae, streptococci, and many strains of staphylococci, including some resistant to other "mycins." Supplied as Capsules, 125 and 250 mg., vials of 36; Oral Suspension, 125 mg. per 5-cc. teaspoonful, bottles of 2 fl. oz.

new

CYCLAMYCIN®

Triacetyloleandomycin, Wyeth

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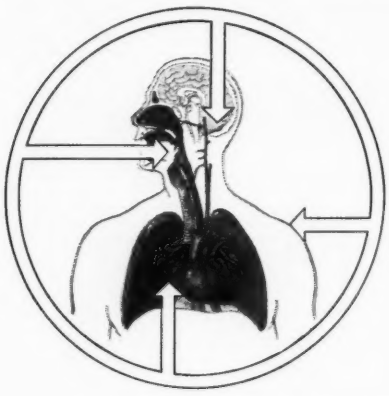
Conforms to Code for Advertising

Wyeth®

Philadelphia 1, Pa.

Now—All cold symptoms can be controlled



Provides Triaminic for more complete and more effective relief from nasal and paranasal congestion because of systemic transport to *all* respiratory membranes—without drawbacks of topical therapy.†

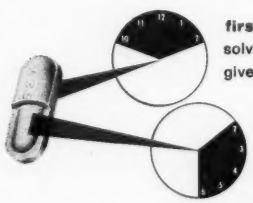
Provides well-tolerated APAP (N-acetyl-p-aminophenol) for prompt and effective analgesic and antipyretic action to make the patient more comfortable.

Provides Dormethan (brand of dextromethorphan HBr) for non-narcotic antitussive action on the cough reflex center in the medulla—as effective as codeine but without codeine's drawbacks.

Provides terpin hydrate, classic expectorant to thin inspissated mucus and help the patient clear the respiratory passages.

†Lhotka, F. M.: Illinois M. J. 112:259 (Dec.) 1957. Fabricant, N. D.: E. E. N. T. Monthly 37:460 (July) 1958. Farmer, D. F.: Clin. Med. 5:1183 (Sept.) 1958.

Special "timed release" design



first—the outer layer dissolves within minutes to give 3 to 4 hours of relief

then—the inner core releases its ingredients to sustain relief for 3 to 4 more hours

also available for those patients who prefer liquid medication: **Tussagesic suspension**

Each TUSSAGESIC tablet provides:

TRIAMINIC®	50 mg.
(phenylpropanolamine HCl	25 mg.
pheniramine maleate	12.5 mg.
pyrilamine maleate	12.5 mg.)
Dormethan (brand of dextromethorphan HBr)	30 mg.
Terpin hydrate	180 mg.
APAP (N-acetyl-p-aminophenol)	325 mg.

Dosage: One tablet in the morning, midafternoon and in the evening, if needed.

Tussagesic* *timed-release tablets*

*Contains TRIAMINIC to STOP running noses and open stuffed noses orally

SMITH-DORSEY • a division of The Wander Company • Lincoln, Nebraska • Peterborough, Canada

- *Prompt remission of symptoms*
- *Bleeding and frequency of stools sharply reduced*
- *Healing of rectal mucosa within a month in most cases*
- *Can be given safely over long periods of time*

Azulfidine®

BRAND OF SALICYLAZOSULFAPYRIDINE

the most valuable drug in the treatment of

Ulcerative Colitis

"The most widely accepted sulfonamide preparation today for the therapy of chronic ulcerative colitis is salicylazosulfapyridine (Azulfidine)."

Hightower, N.C., Jr., and others: Am. J. Digest. Dis., 3:931 (Dec.) 1958

Also valuable in treatment of regional enteritis and other forms of colitis

Pharmacia Laboratories, Inc.
New York City.

Fostex®
treats their acne while they wash

degreases the skin helps remove blackheads dries and peels the skin

...and this is how it works

Fostex provides essential actions necessary in treating acne. It washes off excess oil. It unblocks pores by penetrating and softening blackheads. It dries and peels the skin, removing papule coverings, thus permitting drainage of sebaceous glands.

Fostex contains Sebulytic®,* a combination of surface-active wetting agents with remarkable antiseborrheic, keratolytic and antibacterial actions . . . enhanced by sulfur 2%, salicylic acid 2%, hexachlorophene 1%.

*sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate and sodium dioctyl sulfosuccinate.

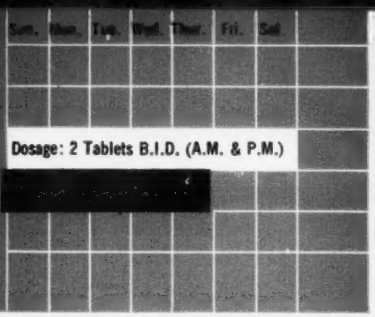
Your patients will like Fostex because it is so simple to use. They simply wash acne skin 2 to 4 times a day with Fostex, instead of using soap.

FOSTEX CREAM . . . in 4.5 oz. jars. For therapeutic washing in the initial phase of oily acne treatment.

FOSTEX CAKE . . . in bar form. For therapeutic washing to keep the skin dry and free of blackheads during maintenance therapy. Also used in relatively less oily acne.

Write for samples.

WESTWOOD PHARMACEUTICALS Buffalo 13, New York



in premenstrual tension only neo Bromth® treats the whole syndrome

It was the introduction of neo Bromth several years ago that created such widespread interest in the premenstrual syndrome—because of neo Bromth's specific ability to prevent the development of the condition in the first place.

The action of neo Bromth is not limited merely to control of abnormal water retention, or of nervousness, or of pain—or any other single or several of the multiple manifestations characteristic of premenstrual tension. neo Bromth effectively controls the *whole* syndrome.

neo Bromth is also completely free from the undesirable side effects associated with such limited-action therapy as ammonium chloride, hormones, tranquilizers and potent diuretics. neo Bromth has continued to prove to be the safest—as well as the most effective—treatment for premenstrual tension.

Each 80 mg. tablet contains 50 mg. Pamabrom, and 30 mg. pyrilamine maleate. Dosage is 2 tablets twice daily (morning and night) beginning 5 to 7 days before menstruation. Discontinue when the flow starts.

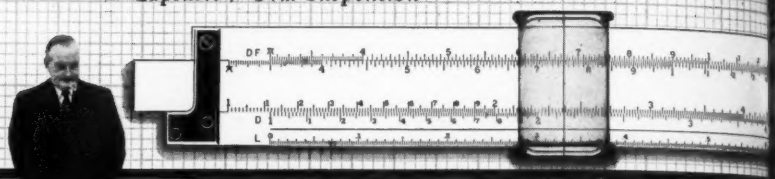
BRAYTEN PHARMACEUTICAL COMPANY • Chattanooga 9, Tennessee

PRONOUNCED TAY-O

℞ Tao* *designed for superior control of common Gram-positive infections*

(triacetyloleandomycin)

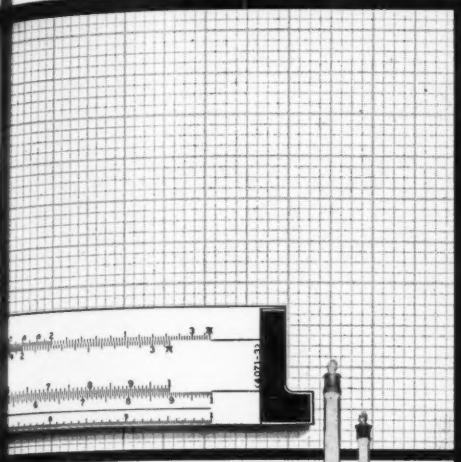
Capsules / Oral Suspension



in the patient:

95% effective in published cases[1-8]

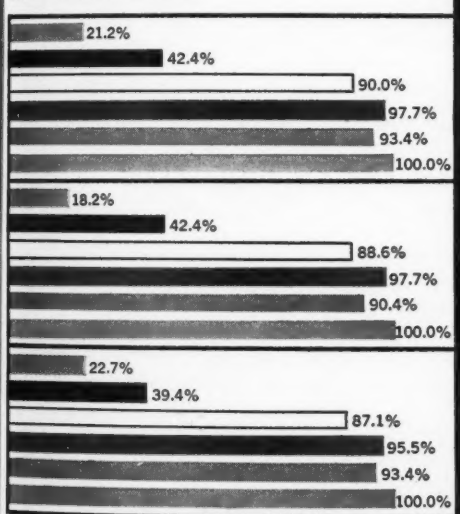
Conditions treated	No. of Patients	Cured	Improved	Failure
ALL INFECTIONS	558	448	80	30
Respiratory infections	258	208	31	19
Pharyngitis and/or tonsillitis	65	58	5	2
Pneumonia	90	66	17	7
Infectious asthma	44	38	–	6
Otitis media	31	29	2	–
Other respiratory (bronchitis, bronchiolitis, bronchiectasis, pneumonitis, laryngotracheitis, strep throat)	28	17	7	4
Skin and soft tissue infections	230	191	38	1
Infected wounds, incisions and lacerations	41	33	8	–
Abscesses	51	43	8	–
Furunculosis	58	51	6	1
Acne, pustular	43	28	15	–
Pyoderma	19	19	–	–
Other skin and soft tissue (infected burns, cellulitis, impetigo, ulcers, others)	18	17	1	–
Genitourinary infections	28	19	3	6
Acute pyelitis and cystitis	10	8	2	–
Urethritis with gonorrhea or cystitis	8	8	–	–
Pyelonephritis	4	1	–	3
Salpingitis	5	1	1	3
Pelvic inflammation with endometriosis	1	1	–	–
Miscellaneous (adenitis, enteritis, enterocolitis, subacute bacterial endocarditis, fever, hematoma, staphylococcus carriers, osteomyelitis, tenosynovitis, septic arthritis, acute bursitis, periarthritis)	42	30	8	4



in the laboratory:

over 90% effective against resistant staph

COMPARATIVE TESTS BY THREE METHODS (DISC, TUBE DILUTION, CYLINDER PLATE) ON 130 STAPHYLOCOCCI[9]



Percentage of organisms inhibited by the range of concentrations listed for each antibiotic.

Other TAO advantages:

Rapidly absorbed—stable in gastric acid,[7] TAO needs no retarding protective coating

Low in toxicity—freedom from side effects in 96% of patients treated; cessation of therapy is rarely required

Highly palatable—"practically tasteless"[7] active ingredient in a pleasant cherry-flavored medium.

Dosage and Administration: Dosage varies according to the severity of the infection. **For adults,** the average dose is 250 mg. q.i.d.; to 500 mg. q.i.d. in more severe infections. **For children** 8 months to 8 years, a daily dose of approximately 30 mg./Kg. body weight in divided doses has been found effective. Since TAO is therapeutically stable in gastric acid, it may be administered without regard to meals.

Supplied: TAO Capsules—250 mg. and 125 mg., bottles of 60. TAO for Oral Suspension—1.5 Gm., 125 mg. per teaspoonful (5 cc.) when reconstituted; unusually palatable cherry flavor; 2 oz. bottle.

References: 1. Koch, R., and Asay, L. D.: J. Pediat., in press. 2. Leming, B. H., Jr., et al.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958. 3. Meliman, et al.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958. 4. Olansky, S., and McCormick, G. E., Jr.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958. 5. Shubin, H., et al.: Antibiotics Annual 1957-1958, New York, N. Y., Medical Encyclopedia, Inc., 1958, p. 679. 6. Isenberg, H., and Karelitz, S.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958. 7. Wennersten, J. R.: Antibiotic Med. & Clin. Therapy 5:527 (Aug.) 1958. 8. Kaplan, M. A., and Goldin, M.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958. 9. Truant, J. P.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958.

TAO dosage forms—for specific clinical situations

TAO Pediatric Drops

For children—flavorful, easy to administer.

Supplied: When reconstituted, 100 mg. per cc. Special calibrated droppers—5 drops (approx. 25 mg.) and 10 drops (approx. 50 mg.). 10 cc. bottle.

TAO-AC (TAO analgesic, antihistaminic compound)

To eradicate pain and physical discomfort in respiratory disorders.

Supplied: In bottles of 36 capsules.

TAOMID® (TAO with triple sulfas)

For dual control of Gram-positive and Gram-negative infections.

Supplied: Tablets, bottles of 60. Oral Suspension, bottles of 60 cc.

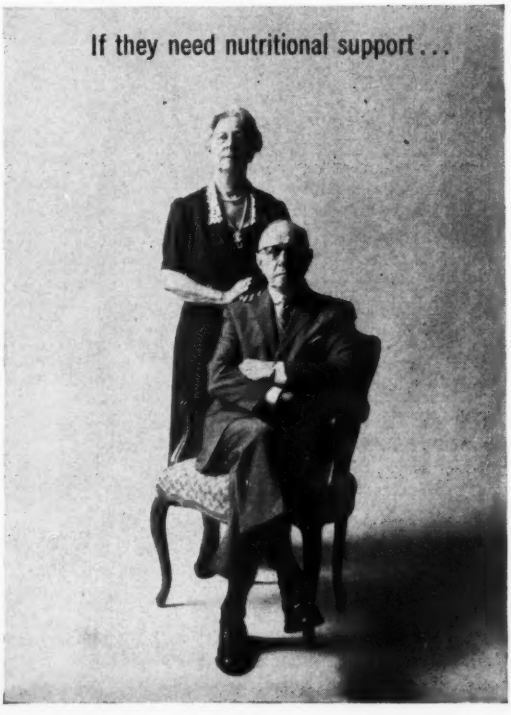
Intramuscular or Intravenous

For direct action—in clinical emergencies.

Supplied: In 10 cc. vials.

®TRADEMARK

New York 17, N.Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being



they deserve

GEVRAL®

Vitamin-Mineral Supplement Lederle

CAPSULES—14 VITAMINS—11 MINERALS

LEDERLE LABORATORIES, a Division of
AMERICAN CYANAMID COMPANY, Pearl River, New York

Lederle

Butazolidin®

(phenylbutazone GEIGY)

tablets · alka capsules **potent · nonhormonal · anti-inflammatory agent**

BUTAZOLIDIN tablets or the Alka capsules are **equally effective but individually adaptable in a wide range of arthritic disorders.**

Recent clinical reports continue to justify the selection of Butazolidin for rapid relief of pain, increased mobility, and early resolution of inflammation.

Gouty Arthritis: "...95 per cent of patients experienced a satisfactory response..."[1]

Rheumatoid Arthritis: In "A total of 215 cases...over half, 50.7 per cent showed at least major improvement, with 21.8 per cent showing minor improvement...."[2] **Osteoarthritis:** 301 cases showed "...a total of 44.5 per cent with complete remission or major improvement. Of the remainder, 28.2 per cent showed minor improvement...."[2] **Spondylitis:** All patients "...experienced initial major improvement that was maintained throughout the period of medication."[3] **Painful Shoulder Syndrome:** Response of 70 patients with various forms showed "...8.6 per cent complete remissions, 47.1 per cent major improvement, 20.0 per cent minor improvement...."[2]

References: 1. Graham, W.: Canad. M. A. J. 79:634 (Oct. 15) 1958. 2. Robins, H. M.; Lockie, L. M.; Norcross, B.; Latona, S., and Riordan, D. J.: Am. Pract. Digest Treat. 8:1758, 1957. 3. Kuzell, W. C.; Schaffarzick, R. W.; Naugler, W. E., and Champlin, B. M.: New England J. Med. 256:388, 1957.

Availability BUTAZOLIDIN® (phenylbutazone GEIGY): Red coated tablets of 100 mg. BUTAZOLIDIN® Alka: Capsules containing BUTAZOLIDIN® (phenylbutazone GEIGY), 100 mg.; dried aluminum hydroxide gel, 100 mg.; magnesium trisilicate 150 mg.; hematropine methylbromide, 1.25 mg.

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ARDSLEY, NEW YORK

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offers four beneficial effects

1. relieves anxiety, tension and related depression
2. exerts a unique alerting effect in many patients
3. dispels preoccupation with emotionally induced symptoms such as headache, g.i. disturbances and non-specific musculoskeletal pain
4. normalizes sleeping and eating habits

WORKING PATIENTS appreciate Compazine's remarkable freedom from drowsiness and the convenient daylong calming effect of a single 'Compazine' Spansule† capsule, taken on arising. Also available: Tablets, Ampuls, Multiple dose vials, Syrup and Suppositories.

SKF SMITH KLINE & FRENCH LABORATORIES

*T.M. Reg. U.S. Pat. Off. for prochlorperazine, S.K.F.
† T.M. Reg. U.S. Pat. Off. for sustained release capsules, S.K.F.

when fear-anxiety
finds its somatic outlet in
cardiac or g.i. symptoms[1]

SYCOTROL

1-piperidine ethanol benzilate hydrochloride

ANTIPHOBIC

without sedative or depressant effect

"...tends to abolish fears and resulting neurotic responses engendered by anxiety and stress. Discrimination and ego functions are not depressed."[1]

Dosage: 1 tablet, 3-4 times daily.

Supplied: 3 mg. tablets in bottles of 100.

Announcing

TWO NEW IMPORTANT MEDICATIONS

FOR THE PEPTIC ULCER TRIAD—
FEAR-ANXIETY, HYPERMOTILITY, HYPERACIDITY

THE
TRI-LOGISTIC
APPROACH

MODUTROL

ANTIPHOBIC
ANTISPASMODIC
ANTACID

the presence of SYCOTROL—a specific for the fear-anxiety component—now makes possible total peptic ulcer therapy

Without rigid dietary restrictions, MODUTROL as the sole medication, gave complete relief in previously resistant cases of peptic ulcer. No untoward side effects were seen even on prolonged therapy.[2]

*Trademark

REED & CARNRICK / JERSEY CITY 6, NEW JERSEY

stop diarrhea

solves acute diarrheal disease problems...

■ swiftly relieves symptoms ■ rapidly destroys bacterial pathogens (bactericidal rather than bacteriostatic) ■ succeeds where others fail against the enteric "problem pathogens" — increasingly prevalent, refractory strains of Staphylococcus, Escherichia, Salmonella and Shigella

...without creating new problems

■ does *not* upset the balance of normal intestinal flora
■ does *not* encourage monilial or staphylococcal overgrowth
■ does *not* induce significant bacterial resistance

Furoxone®

BRAND OF FURAZOLIDONE

liquid

A PLEASANT ORANGE-MINT FLAVORED SUSPENSION containing FUROXONE, 50 mg. per 15 cc., with kaolin and pectin ■ For patients of all ages (may be mixed with infant formulas, passes through a standard nursing nipple) ■ Dosage: Should provide (in 4 divided doses) 400 mg. daily for adults, 5 mg./Kg. daily for children ■ Supplied: bottles of 240 cc. (also: FUROXONE Tablets, 100 mg. scored, bottles of 20 and 100)

THE NITROFURANS—a unique class of antimicrobials
EATON LABORATORIES, NORWICH, NEW YORK

REACHING FOR THOSE 9B's NEARLY PUT ME ON THE SHELF...

Reaching for 9B shoes and other top shelf sizes is no joke . . . it gave me a terrible kink in my back.

Before the day was over, I could hardly stoop to push a shoehorn.

I called my doctor that night and picked up the tablets he prescribed.

The pain went away fast—in just 15 minutes—and I was back on the job the next morning! But not one 9B customer came in the whole day!

Percodan®-Demi & Percodan® *Tablets*

Salts of Dihydrohydroxycodeinone and Homatropine plus APC

FOR PAIN

ACTS FASTER — usually within 5-15 minutes. LASTS LONGER — usually 6 hours or more. MORE THOROUGH RELIEF — permits uninterrupted sleep through the night. RARELY CONSTIPATES — excellent for chronic or bedridden patients. VERSATILE — new "demi" strength permits dosage flexibility to meet each patient's specific needs. PERCODAN-DEMI provides the PERCODAN formula with one-half the amount of salts of dihydrohydroxycodeinone and homatropine.

AVERAGE ADULT DOSE: 1 tablet every 6 hours. May be habit-forming. Federal law permits oral prescription.

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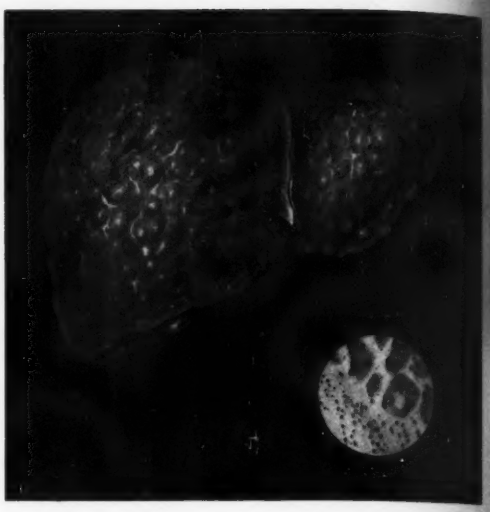

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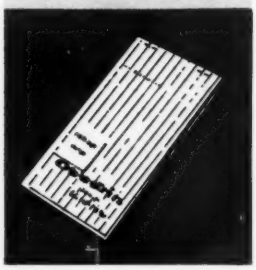

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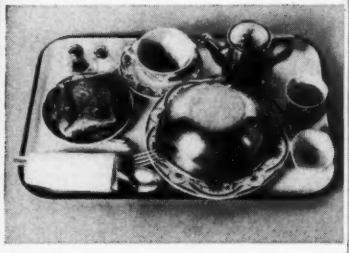

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1. "Present Status of the Problem of the Porphyrias"
2. "Inherent Functional Disabilities—Relative Excretory Inability for Iron, and Problems of Sideropenia and Cytosiderosis"
3. "Inherent Functional Disabilities—Relative Excretory Inability for Uric Acid, and Problem of Gout"

John B. Hickam, M.D., Chairman, Department of Medicine, Indiana University Medical Center
1. "Advances in the Evaluation of Pulmonary Function"
2. "The Circulation of the Optic Fundus in Cardiovascular Disorders, as Observed by a New Method"
3. "New Data in the Field of Pulmonary Failure and Cor Pulmonale"

Joseph E. Murray, M.D., Clinical Associate in Surgery, Harvard School of Medicine and Massachusetts General Hospital
1. "Facial Fractures and Deformities"
2. "Organ and Tissue Homotransplantation—Physiological and Immunologic Considerations"—Part I
3. "Organ and Tissue Homotransplantation"—Surgical Considerations—Part II

Maurice N. Richter, M.D., Professor of Pathology and Chairman of the Department of Pathology, Postgraduate Hospital, New York City
1. "Interrelationships of the Lymphomas"
2. "Pathology of Hypersplenism"
3. "Indications for Splenectomy from the Standpoint of Splenic Pathology"

A. Earl Walker, M.D., Professor of Neurosurgery, The Johns Hopkins University
1. "Surgical Experiences in and About the Brain Stem"
2. "Neurosurgical Approach to Intractable Medical Conditions"
3. "Surgical Consideration of Neck Pain"

Paul Wood, O.B.E., M.D., F.R.C.P., Director, Institute of Cardiology, London; Physician to the National Heart Hospital and Brompton Hospital, London
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Table 1.

No. of Patients	Results	Percent
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11,201	Good	51.1%
2,802	Fair	12.8%
1,088	Unsatisfactory	5.0%
622	Side effects	3.0%

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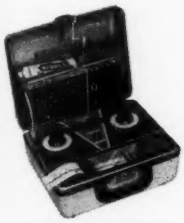

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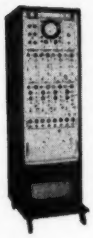

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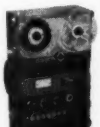

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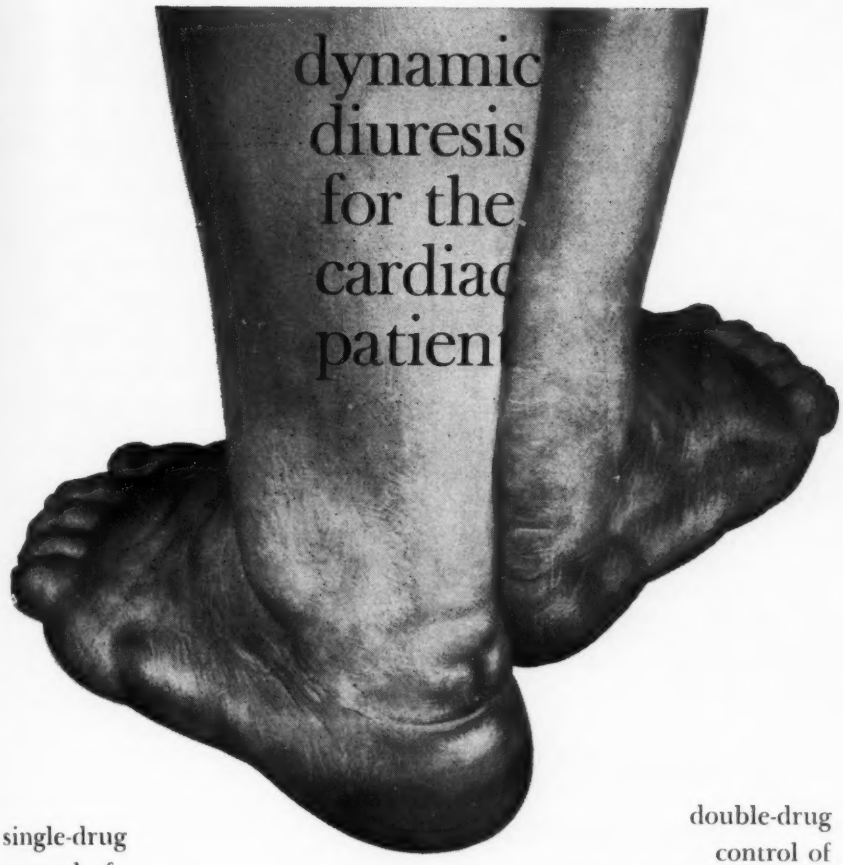

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The Tongue*

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The anatomy and physiology of the tongue are reviewed very well. The consideration of the diseases of the tongue is broad with valuable discussion of differential diagnosis.

ONE MIGHT SAY that, like the horse and buggy, detailed interest in the tongue as a guide to diagnosis has given way to modernization. Modernization in this case being the laboratory.

No longer is so much emphasis placed on the information which could be obtained from the order, "stick out your tongue." Whether this provided the practitioner with valid information or just the opportunity to organize his thinking is a matter of conjecture.

However, if one is provided with modern tools and there is still doubt about a diagnosis, a review of the subject is in order. The puzzling stimulation provided by a single microscopic slide, from which several men could not make a diagnosis, provided the curiosity for the present consideration of the tongue.

The tongue is a no man's land of medicine. It is an orphan not claimed by surgery, ear, nose, and throat, internists, dentists, or dermatologists. This is in contrast to the penis where the urologist is its champion or the lower bowel and anus where the proctologist has set aside a separate specialty dealing with this limited area.

Embryology and Anatomy

"Developmentally the tongue is a mucous membrane sac which becomes stuffed with voluntary muscle."[1]

All of us vaguely recall from our medical school days that certain portions of our head and neck are derived from branchial arches and clefts which compare with the gills on a fish. Very early in embryonic life portions of the first and second branchial arches differentiate into the right and left lingual swellings which fuse to form the anterior two-thirds of the tongue. This is joined by elements of the second, third and fourth branchial arches forming the root or base of the tongue. An embryonic protuberance lying between the first and second arches and referred to as the tuberculum impar probably forms the median rhomboid area.

The body and root of the tongue are demarcated from each other by a "V" shaped groove, the sulcus terminalis. At the apex of this "V" shaped groove, there is normally a blind pit or dimple, the foramen caecum. This represents the site of the thyroid evagination, the point of origin of the thyroglossal duct, which usually atrophies in early embryonic life.

Anterior to the sulcus terminalis the mucous membrane is considered as ectodermal in origin, and posteriorly it is entodermal, with the base of the tongue actually forming the anterior wall of the oral pharynx.

Each portion of the tongue retains the sensory innervation of its corresponding embryologic branchial arch. The twelfth cranial nerve (hypoglossal) supplies the motor innervation for the musculature of the tongue. This innervation lends strong support to the contention that the tongue muscles have migrated upward from occipital somites or segments.

*Read before the Section on Dermatology and Syphilology, Southern Medical Association, Fifty-Second Annual Meeting, New Orleans, La., November 3-6, 1958.

Butlin[2] considered the tongue to be divided anatomically and functionally into two parts. Dorsally a lingual muscular organ and ventrally a sublingual organ characterized by mucous and serous salivary glands. It is only this glandular or sublingual tongue which is found in the lower vertebrates. He contends that the muscular substance migrates from lower dermatomes, growing forward, pushing aside the glandular structures which now lie below or to the side of the tongue in humans. In this process the simple tubular glands, like those lining the stomach and intestines, are transformed into compound glands (sublingual and submaxillary) which can be compared to the pancreas.

The rudimentary serous glands (Von Ebner) are more intimately related to the taste buds in the region of the sulcus terminalis with the mucous or mixed compound glands more abundant as organized structures elsewhere on or below the tongue. On the ventral surface, anteriorly are the glands of Nuhn or Blandin (mixed mucous and serous glands), and below the tongue the sublingual glands which are predominantly mucous secreting glands. The submaxillary gland empties (via Wharton's duct) on either side of the base of the frenulum linguae, by a common ductal opening with the sublingual glands.

The extrinsic muscles extend into the tongue from bony attachments, giving the tongue a degree of stability or fixation. Intrinsic muscles of the body and root of the tongue extend longitudinally, transversely and vertically providing the tongue with a wide range of motion. These muscle fibers are partially separated by a median fibrous septum. This septum is incomplete and permits the crossing of muscle fibers from one-half of the tongue to the other. There is little communication of blood vessels across the midline but there is a free anastomosis of the lymphatics. This septum, while incomplete, does however act as a partial barrier, when one considers that infections and primary carcinoma do not tend to cross the midline. The occasional metastasis of carcinoma of the tongue to the opposite side can be explained by the free anastomosis of the lymphatics in the tongue and in the neck.

The epithelium of the tongue differs from other mucosal surfaces because of the lack of a well developed submucosal connective tissue layer or dermis. The stratified squamous epithelial covering is therefore intimately or directly related or bound to the underlying musculature, being separated only by a thin tough lamina propria. This accounts for the difficulty of securing anesthesia when local anesthetic agents are injected.

The characteristic rough appearance of the dorsal surface of the normal tongue is due to numerous small projections, the lingual papillae. The papillae have been designated as filiform (thread-like), fungiform (toad stool-like), and circumvallate types. Two lesser known varieties are the conical and foliate papillae which are, however, distinct anatomic entities. Functionally, the papillae act as taste and touch receptors. The unusual appearance of a hairy tongue, whether black, brown or yellow is a result of the overgrowth or retention of the keratinous portions of the filiform papillae. These are most numerous in the median rhomboid area.

Function

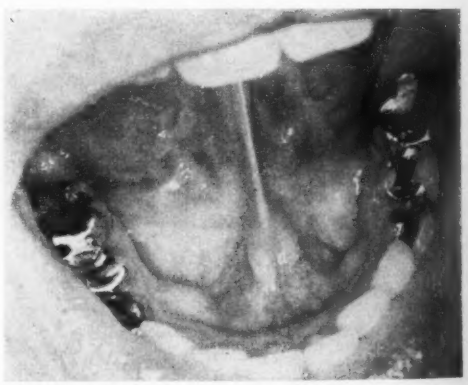
The tongue plays an important role in swallowing (deglutition), chewing (mastication), taste (gustitation), and speech (phonation). To these, the less important functions of absorption, beginning digestion and whistling should be added.

Diseases or Abnormalities of the Tongue

CONGENITAL

Any discussion of diseases or abnormalities of the tongue will include the congenital

FIG. 1



Ankyloglossia, "tongue tie" persisting in adult life.

anomalies. Some of these may be seen in any given person's medical life span but some are so rare as to be considered as of historical interest or as medical oddities. Of this later group the following are referred to in medical literature, some of them admitting to a single case report.

Aglossia or congenital absence of the tongue is limited to an absence of the anterior portion or body of the tongue. No cases have been reported where the root of the tongue is absent. Congenital fusion of the body of the tongue with the floor of the mouth does not belong in this category.

Microglossia is a rare condition where there is poor development of the body of the tongue.

Bifid or cleft tongue, as a normal organ, is found in certain mammals (seal), in certain birds (the raven), and is well developed in reptiles. Developmentally the fusion of the right and left lingual swellings in the embryo would seem to predict a more frequent occurrence of this anomaly, but it is nevertheless rare.

Abnormally long tongues have been reported as having such extensibility that they reach the chest or the tip of the chin.

Excessive mobility of the tongue produces tongue swallowing which is reported in infants as a cause of strangulation and suffocation.

Congenital fissuring and congenital absence of papillae has been reported as isolated rare anomalies.

FIG. 2

Hemangioma of tongue producing macroglossia in an adult.

FIG. 3

Lymphangioma of tongue with typical "frog spawn" or "glass bead" appearance.

The following are congenital anomalies of the tongue which are more likely to be encountered in a medical life span.

Ankyloglossia or tongue tie (Fig. 1) may involve the attachment of the tongue to the gums (gingiva), roof of the mouth or a simple shortening of the frenulum linguae. Injudicious treatment of this condition can cause serious hemorrhage or asphyxia from "tongue swallowing."

Hemangiomas (Fig. 2) may be localized or may involve the entire body of the tongue.

Lymphangiomas (Fig. 3) may present themselves as lymphangioma circumscriptum (lymphangiokeratoma) or a diffuse lymphangiomatous involvement related to hygroma.

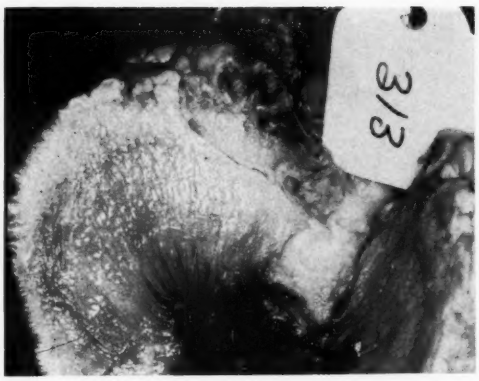
Thyroglossal duct cysts (Fig. 4), when they occur usually in relation to the foramen caecum, are primarily a surgical problem. Myxedema has been reported following removal of thyroglossal duct cysts and ectopic thyroid tissue in cases where no thyroid tissue could be found in the normal location in the neck.

Congenital cysts of glandular structures (Fig. 5) may be of such dimension that they present the appearance of double tongue. Some of these are dermoid cysts, which differ from the acquired retention cyst or ranula.

ACQUIRED

Treponemal infection (syphilis) may in-

FIG. 4



Persistence of thyroglossal duct with ectopic thyroid tissue present in the root of the tongue. (Incidental finding in postmortem specimen.)

volve the tongue as primary, secondary, or late benign lesions.

Bacterial infections with staphylococcal, streptococcal, gonococcal, tuberculosis, diphtheria and Vincent's infection are all capable of involving the tongue and oral cavity.

Mycotic infections of moniliasis or thrush *(Candida albicans),* actinomycosis and histoplasmosis are all well known.

Viral diseases such as herpes, chickenpox, smallpox, and epidemic stomatitis (hoof and mouth disease) may involve the tongue as part of the over-all disease. The problem of herpetic gingivostomatitis is only now beginning to be appreciated as a separate problem especially in children.

Certain *inflammatory diseases,* urticaria, lichen planus, geographic tongue, erythema multiforme particularly the bullous or erosive type often involve the tongue.

Allergic reactions to foods, especially walnuts, chicken, cheese, sea food, chocolate and pork have all been reported. Likewise there are reports of contact dermatitis of the tongue from lipstick and dentrifices.

Physical agents such as pencils, teeth, bullets, bone splinters, pipe-stems, hot foods, caustics, acids and galvanic current can all produce injury to the tongue.

Psychologic stress, animal parasites, systemic disease, vitamin deficiency, metabolic disease, aging processes, and a host of miscellaneous conditions can produce disease with manifestations on the tongue.

The tongue is also the site of certain *tumors,*—benign, malignant or metastatic. The most common tumor is squamous, epidermoid, or prickle-cell carcinoma.

It is impossible to cover the entire group of interesting conditions of the tongue in detail in a short time. More detailed consideration will therefore be given to only a few which are of great general interest but of particular interest to the dermatologist and oral and dermal-histopathologists.

Macroglossia. In the past few years macroglossia has been a feature in over-all disease where the dermatologists' assistance has been most helpful to tumor boards and fellow physicians.

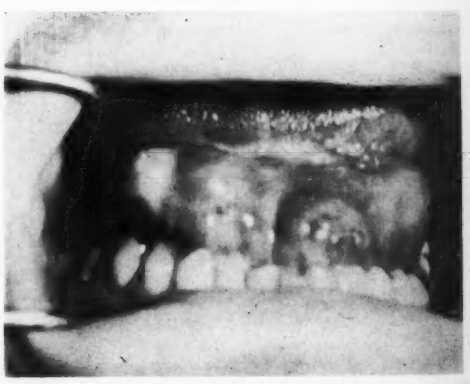
The protruding tongue of the mongoloid idiot may not be a true macroglossia but may result from alterations of the bony structures of the palate and jaw, making the oral cavity too small for the tongue.

Certain endocrine disturbances likewise have an associated macroglossia. Of these cretinism, myxedema and acromegaly are all familiar.

The growth of malignancies can attain such proportions that the tongue can no longer be contained within the oral cavity. Of these rhabdomyosarcoma, and squamous cell carcinoma are good examples. Infiltration of the tongue in malignant lymphomas can occur and produce macroglossia.

The disposition of vascular or angiomatous lesions capable of producing macroglossia are often presented for opinion to practitioners

FIG. 5



Congenital cyst of glandular structures giving the impression of a "double tongue."

FIG. 6

Granular cell myoblastoma of the tongue.

or members of tumor boards. A relatively common problem is the selection of the best method for treating hemangiomas of the tongue. Here there is more general agreement on the modalities to be used, surgery, radium or x-ray therapy, or injection of sclerosing agents, because of greater familiarity with this type of lesion. However, when one is presented with a lymphangioma, a relatively rare lesion, the dermatologists' opinion is more apt to be solicited. Most physicians and dentists are almost completely unfamiliar with a condition that carries the name or diagnosis of lymphangioma circumscriptum, lymphangiokeratoma, cavernous lymphangioma or hygroma.

Case report (Fig. 3). A 5 year old girl of Mexican descent was seen because of an anomalous condition of her tongue which was noted shortly after birth. From the photograph one can plainly see why such descriptive words as "frog spawn," "glass bead," cystic, translucent, bluish or vesicular are all used to describe this lesion. When biopsy was performed the tongue was held firmly between the fingers with gauze.

Probably as a result of this trauma the tongue became much larger, and within a few hours it was so large she could not retract it into her mouth. This frightening complication persisted for 3 weeks and began to subside coincident with the administration of large doses of vitamin A. The rationale for the use of vitamin A by the resident physician was based on the fact that there was a keratotic element to the lesion and he thought this vitamin might beneficially affect at least this one component. Quite possibly, however, it was the trauma of pressure on the tongue at the time of biopsy, with resultant rupture of lymph vessels and subsequent sclerosis which accounted for the partial involution.

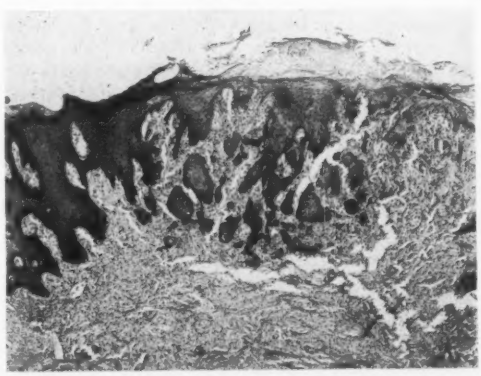
The microscopic sections show lymphangioma with elements of lymphangiokeratoma. There is also a marked piling up of fibrin over the angiomatous projections at the margin of the tongue. Many cases of lymphangioma of the tongue require radiation or surgical intervention because of the increasing macroglossia.

We dermatologists will infrequently be required to differentiate two conditions which present macroglossia, inability to extend the tongue, hoarseness of the voice, and skin changes elsewhere. These are systemic amyloidosis (usually primary) and lipoid proteinosis (hyalinosis cutis et mucosae).[3] The histopathologic changes in these two conditions are particularly helpful when combined with other clinical data.

Granular cell myoblastoma[4] of the tongue (Fig. 6) is considered separately because it is a relatively common tumor and it demonstrates better than any other, the absolute need for performing a deep biopsy on tongue lesions. If the biopsy is poorly or inadequately done it could result in a mistaken diagnosis necessitating a serious and deforming operation.

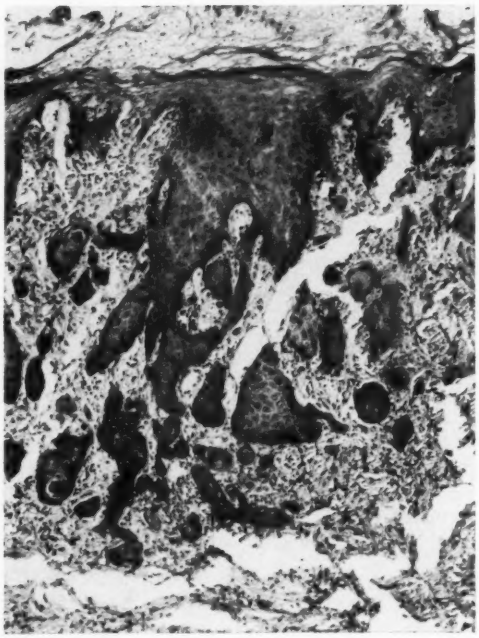
This lesion often presents itself as an asymptomatic nodule on the dorsum of the tongue. The clinician knows at the outset that the diagnosis rests on the pathologic examination of the tissue. Microscopically the degree of pseudo-epitheliomatous hyperplasia overlying the granular cells is indistinguishable from squamous cell carcinoma until the underlying granular cells are recognized as the factor stimulating the changes in the epithelium[5] (Figs. 7-10). Often within the pseudo-epitheliomatous processes there is also

FIG. 7



Note the extreme degree of pseudo-epitheliomatous hyperplasia of the epithelium over myoblastoma of the tongue.

FIG. 8



The benign pseudo-epitheliomatous hyperplasia in myoblastoma mimics squamous cell carcinoma as evidenced by "pseudo-malignant dyskeratotic phenomena" in the form of epithelial pearls, individual cell keratinization and variation in staining.

pseudo-keratinization of individual cells, pseudo-pearl formation, pseudo-invasion and variation in staining. These changes are shown in the photomicrographs along with the typical granular cells.

Technic of biopsy. The problem of the biopsy of tongue lesions can be reduced by inserting a large curved threaded needle, deep in the tissue at the site to be biopsied after the tissue has been anesthesized. With a sharp knife one can cut deeply to the level of the needle, remove the tissue, pull the threaded needle through the tissue and immediately control the bleeding by tying the suture. The presence of the needle in the tissue before biopsy also provides a point of fixation for holding the tongue, which is an additional advantage in this freely movable organ.

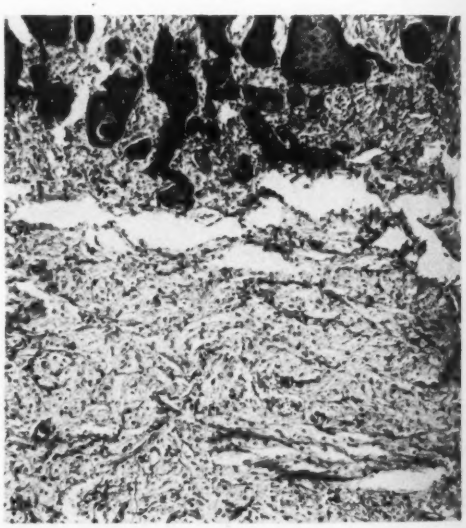
Emergencies as related to the tongue. As a final consideration it is in order to discuss emergency conditions.

It is conceivable that any bacterial infection of the tongue could produce a sufficiently rapid increase in size due to the edema, and to present an obstruction to breathing and swallowing. When this occurs an emergency exists and prompt action is necessary. Abscesses or cellulitis of the tongue fall in this category.

The presence of large foreign bodies in the tongue following accidents, where bone, splinters of wood, pipe-stems or other similar extraneous matter are found in the tongue, present a surgical emergency. Butlin[2] stresses the absolute necessity of being prepared to do extensive and lifesaving surgery to control hemorrhage. He cites a case of a man who had a four inch piece of pipe-stem embedded in his tongue for four days with increasing pain and swelling. When he was admitted to the hospital, the removal of this foreign body resulted in death from massive hemorrhage within a few minutes. At postmortem examination the pipe-stem which had been present in his tongue for four days were found to have severed the carotid artery and superior vena cava. While it was still embedded it acted as a plug, but upon removal the unexpected hemorrhage could not be controlled, resulting in his almost immediate death. Fatal hemorrhage has recently been reported following the accidental severing of the lingual artery by a dental drill while the dentist was preparing a tooth for the insertion of a full crown.

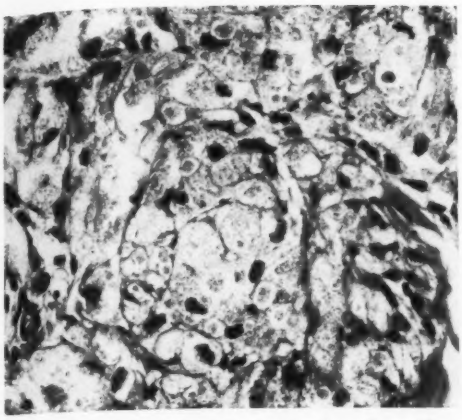
Accidents involving amputation or partial amputation are likewise emergencies both

FIG. 9



Biopsy of tongue lesions must be deep enough to incorporate the granular cell component to prevent errors in diagnosis.

FIG. 10



Typical appearance of the cells, in granular cell myoblastoma.

from the standpoint of repairing the tongue and controlling the hemorrhage.

Severe lacerating injuries to the floor of the mouth, or as in automobile accidents where the mandible is severely shattered, may result in separation or evulsion of the attachment of the genioglossus muscle. Since all of the other muscles are exerting their normal tension, this results in a falling or pulling back of the tongue into the throat causing tongue swallowing and may result in suffocation. This is the same emergency which exists with deep anesthesia when relaxation of the extrinsic muscles of the tongue permits "tongue swallowing."

Urticaria or angioneurotic edema can be of such a degree that tracheotomy will have to be done. This problem has been materially reduced with the use of intravenous antihistamines, intravenous steroids and epinephrine.

Lastly, and probably most dramatic, is the sudden edema of the tongue, often associated with collapse, which is produced by the sting of a wasp, hornet, bee or similar insect accidentally incurred when a person bites into a piece of fruit with the insect on it. In a person specially allergic to this venom this is an acute emergency, and might necessitate prompt tracheotomy. Here again the intravenous use of the antihistamines, steroids or epinephrine are most helpful if available.

Summary

The importance of the tongue and general lack of interest in this organ is stressed.

The congenital anomalies of the tongue have been presented.

Consideration is given to the usual causes of macroglossia.

Special emphasis is placed on the necessity of adequate biopsy of tongue lesions with particular reference to granular cell myoblastoma. A method of controlling bleeding when performing a biopsy on the tongue is outlined.

A group of emergencies of the tongue is enumerated.

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The Prognosis in Acute Myocardial Infarction*

ROBERT L. McMILLAN, M.D., and
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Every clinician knows the many fallacies which beset an attempt at prognosis in serious disease. This is surely true in the case of myocardial infarction. The author believes certain electrocardiographic changes may be of aid in judging the outcome.

IT HAS LONG SINCE BEEN RECOGNIZED THAT, when all cases of acute myocardial infarction are considered, accuracy of prognosis—either favorable or unfavorable—is impossible. A sizable number of patients whose general and cardiac findings seem satisfactory dies suddenly. At the same time it is a common experience to have patients survive for long years of useful living, who gave every appearance of impending death during the early hours or days of acute myocardial infarction.

It has been stated that, "The prognosis is made worse in coronary thrombosis by the following findings: advanced age, a state of shock, an abrupt and prolonged marked fall in blood pressure, duration of severe substernal pain for more than twenty-four hours, fever for a week or more, especially when high at the onset (103 to 104° F.), a high leukocytosis, especially if maintained for more than a week, rapid and marked cardiac dilatation, gallop rhythm, ventricular paroxysmal tachycardia, heart block, pulsus alternans, pulmonary edema with or without cardiac asthma, dropsy and embolic phenomena."[1] A general consideration of these findings as single factors and, more convincingly, when they occur in combination, leads one to believe that they are influenced by the size of the myocardial infarct. Rules of thumb are, at best, notoriously poor in the field of medicine. Nevertheless, it might be stated with a great degree of truth that the more extensive the myocardial infarct, the higher the fever, the greater the leukocytosis and sedimentation rate, the more severe and prolonged the pain, the greater the degree of hypotension or collapse of the circulation, and the more serious the extent of left ventricular dilatation, pulmonary vascular congestion and over-all cardiac failure. One must add to the cases exhibiting the above those who, with or without the opportunity to express themselves, have one pain and fall dead.

A method for measuring quantitatively the severity (and ultimate prognosis) in myocardial infarction was proposed by Schnur,[2] in 1953. In this article arbitrary figures were assigned to complications of infarction such as shock "40," congestive heart failure "20 to 25," concurrent other diseases "10 to 30." He valued arrhythmias from occasional premature ventricular contractions "10" to paroxysmal ventricular tachycardia "40," and found that when the sum of the combined complications totaled 80 or more there was an immediate 95% mortality; a total of 60 to 79 produced an 80% mortality; 40 to 59 a 35% mortality and 20 to 39 a 25% mortality.

It has been said that the "physician who makes a prognosis when he is not forced to do so is a fool."[3] Nevertheless, our purpose is to present certain electrocardiographic findings which, in a high percentage of cases, point to a *poor* prognosis, and to offer a few suggestions which may prevent early death in many of these individuals.

TABLE 1

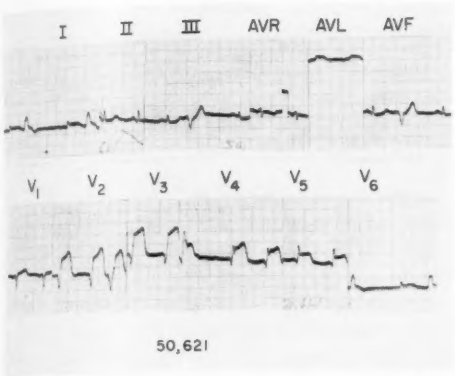
POOR PROGNOSIS IN ACUTE MYOCARDIAL INFARCTION

Total cases predicted early death	46
Total dead within 36 hours	42
Total accuracy of prediction	90%

*Read before the Section on Medicine, Southern Medical Association, Fifty-Second Annual Meeting, New Orleans, La., November 3-6, 1958.

†From the Department of Internal Medicine, Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C.

FIG. 1



J. P. Y. (50621) Male diabetic, age 59. EKG made 2 hours after onset of severe chest pain. Note the early extensive elevation of the S-T segments in leads V2 through V5. Patient died within 36 hours from uncontrolled shock.

Electrocardiographic Studies

Without other revealing information, these cases were selected during the five years from 1953 to 1958 solely on the merits of their electrocardiograms and assigned a code number in a private file designated "impending death." Of an over-all total of 26,000 electrocardiograms, made in the Heart Station of the North Carolina Baptist Hospital from 1953 to 1958, 46 cases fell into the category of "impending death." Of this number 41 died in less than 24 hours and one other patient died 36 hours after the prognosis of imminent death was made. Thus, the prediction of immediate mortality was correctly made in 42 or 90% of the cases (Table 1).

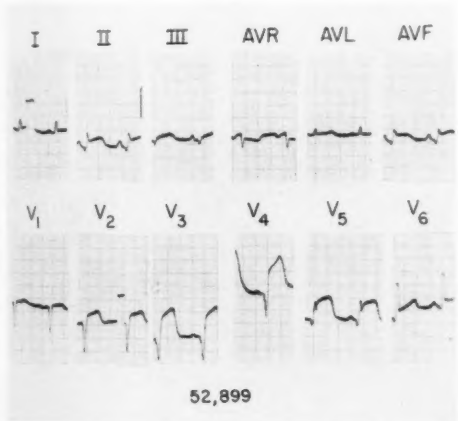
In an attempt to evaluate the factors which influenced the prediction of sudden death, it seems wise to divide the cases into two main groups: (A) Those which presented early electrocardiographic evidence of severe, extensive myocardial damage, and (B) those with disorders of the cardiac rhythm which are generally regarded as of grave significance.

Group A. An analysis of this group of 16 patients reveals that the most significant changes in the electrocardiogram are displacements of the S-T segments.

In the anterior type of acute myocardial infarction two abnormalities are consistently evident. These are the unusual degree of S-T segment elevation in the leads primarily affected in anterior infarction, and the finding of such changes in not only the standard bipolar and unipolar limb leads, but also throughout the extent of leads V1 through V6. In most cases there is an extreme degree of reciprocal depression in leads 3, AVF and often in limb lead 2. Representative examples of the anterior type of acute myocardial infarction are shown in figures 1 and 2.

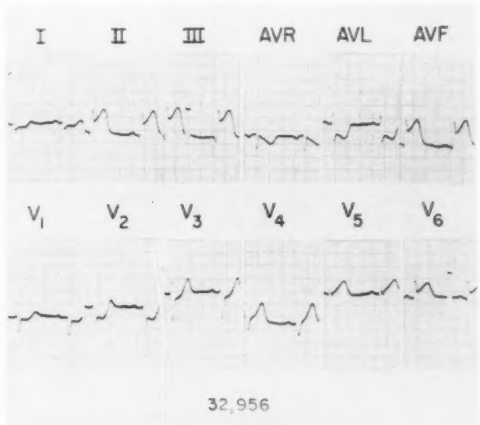
The posterior type of acute myocardial infarction, by similar reasoning, shows extreme

FIG. 2



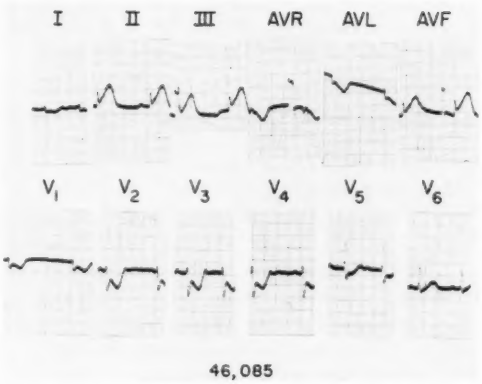
A. E. (52899) Woman, age 70. EKG made 4 hours after the onset of severe chest pain. Extreme elevation of the S-T segments is noted in leads V2 through V6 as well as in leads 2 and AVF, suggesting involvement of the interventricular septum. The patient died 24 hours after onset with intractable shock and pulmonary edema.

FIG. 3



F. L. B. (32956) Man, age 61. EKG made one hour after onset of severe chest pain extending into both arms, neck, and jaw. Note the extreme early elevation of the S-T segments in leads 2, 3, AVF and V6. There is reciprocal depression of the S-T segments in leads 1, AVL, and V1, 2 and 3, most marked in lead AVL. This patient died suddenly while asleep 3 hours after onset.

FIG. 4



R. E. H. (46085) Man, age 61. EKG made 2 hours after onset of severe chest pain. Extreme elevation of the S-T segments is seen in leads 2, 3, and AVF. Marked reciprocal S-T segment depression is noted in leads 1, AVL and V1 through V5. Death occurred suddenly about 70 minutes after the above recording with precipitous ventricular fibrillation and cardiac standstill.

elevation of the S-T segments in limb leads 2, 3 and AVF, and in some cases V5 and V6. There is pronounced reciprocal depression in limb leads 1, AVL, and precordial leads V1-V6. These changes are exemplified in figures 3 and 4.

It is worthy of mention that 13 or 81.3% of the 16 patients in Group A died as predicted (Table 2). However, figure 5 shows the electrocardiogram of one of the 3 survivors. It is noted that the S-T segment

TABLE 2

GROUP A

ELECTROCARDIOGRAPHIC EVIDENCE OF EXTENSIVE MYOCARDIAL DAMAGE

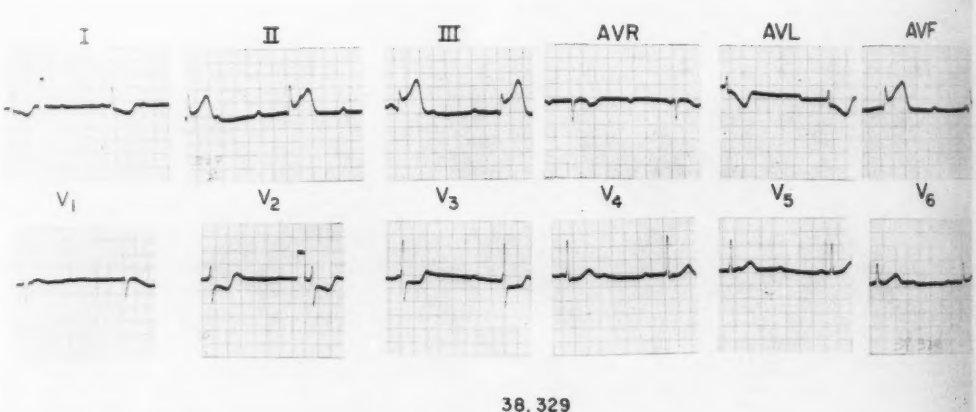
Total cases	16
Death in 36 hours	13
Accuracy of prediction	81%

changes are equally as severe as they were in those who suffered immediate death. This patient also had complete atrioventricular block.

Group B. Of the 31 patients in this category (comprising those of the series having disorders of the cardiac rhythm which are generally regarded as of grave significance) 15 had frank electrocardiographic evidence of acute myocardial infarction. In the remaining 16 patients classical clinical evidence alone warranted the diagnosis of acute myocardial infarction.

In the former group the abnormal rhythms consisted of frequent short paroxysms of ventricular tachycardia and ventricular fibrillation, interrupting normal sino-atrial rhythm (4 patients). Six patients developed paroxysmal atrial fibrillation shortly following the onset of the infarction. One patient had complete heart-block with multifocal premature ventricular contractions. In addition to the above there were 4 patients with left bundle branch block, 2 of which had sino-atrial

FIG. 5



D. P. C. (38329) Man, age 67, known to have chronic lymphocytic leukemia. EKG made 2 hours after onset of severe chest pain. There is marked elevation of the S-T segments in leads 2, 3 and AVF. Pronounced reciprocal depression of the S-T segments is noted in leads 1, AVL and V2 and 3. Also present is complete heartblock which reverted to normal following administration of barium chloride. This patient was alive and active physically 2 years and 3 months after onset.

TABLE 3

GROUP B

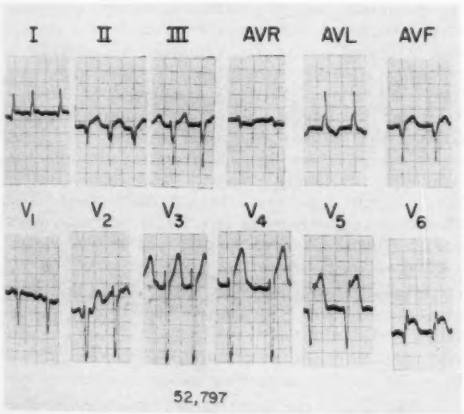
PATIENTS WITH ELECTROCARDIOGRAPHIC FINDINGS OF ARRHYTHMIAS OF GRAVE SIGNIFICANCE

Total grave arrhythmias	31
Obvious extensive myocardial damage	16
Typical clinical acute infarction	15
Total deaths in 24 hours	30
Accuracy of prediction	97%

tachycardia. One had complete heart block, and the fourth had sino-atrial rhythm with variable pathways of ventricular conduction. The immediate mortality of this group was 93.3 per cent (Table 3). The sole survivor of this group had left bundle branch block with sino-atrial tachycardia. Figure 6 is an example of this group.

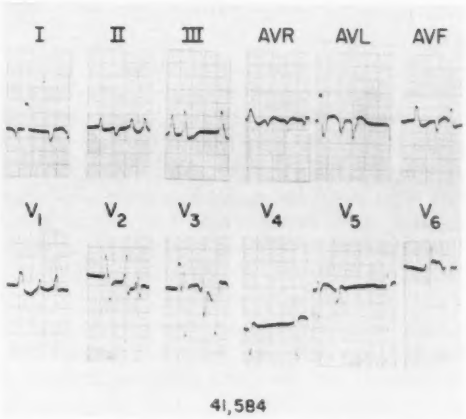
The 16 remaining cases, which compose the latter group referred to above, presented histories of the sudden onset of severe crushing chest pain, often with radiation to both shoulders and arms. In each case, where recorded, the temperature was subnormal, and in all cases profound vascular collapse was present. The electrocardiograms obtained from each of the patients offered no typical findings of acute myocardial infarction, but rather successive multifocal premature ventricular contractions, usually with paroxysmal ventricular tachycardia and paroxysmal ventricular fibrillation. Figure 7 is representative of this group. Death occurred within an hour after the electrocardiogram was recorded in each of these patients.

FIG. 6



D. M. S. (52797) Man, age 47. EKG made one hour after onset of severe chest pain. This record shows atrial fibrillation which developed shortly before the tracing was made. Also present is extreme elevation of the S-T segments in the V leads indicating early anterior myocardial infarction. Death occurred in 2 hours from rapidly progressive vascular collapse.

FIG. 7



L. E. H. (41584) Woman, age 66. EKG made one and one-half hours after onset of severe chest pain. The record shows multiple ectopic ventricular contractions, ventricular tachycardia and ventricular fibrillation occurring paroxysmally. Death occurred 30 minutes following this recording.

It is advocated that patients exhibiting the electrocardiographic findings as presented, early after the occurrence of myocardial infarction be placed in the category of acute medical emergency. Such patients should be placed on the critical list and the responsible relatives notified. A vigilant routine must be instituted, requiring observation of the blood pressure, heart sounds and cardiac rhythm every five minutes or oftener, as the situation might warrant. Relentless, even though gradual, fall in the blood pressure demands prompt measures to prevent shock (collapse). Suitable apparatus for the administration of intravenous drugs should be installed and a slow infusion of 10% glucose in distilled water started. This will facilitate the immediate use of vasopressor substances such as levo-arterenol (Levophed), mephentermine sulphate (Wyamine), metaraminal bitartrate (Aramine), epinephrine, whole blood, or plasma.

Premature ventricular contractions, especially if successive or multifocal, are the usual harbingers of an idioventricular rhythm which may result in ventricular fibrillation and sudden death. Such arrhythmias occur as the mechanism of death from any medical cause whether the basic lesion is cardiac or

not. Therefore the development of these rhythms in any form demands their abolition with procaine amide (Pronestyl) one to two grams intravenously, for immediate control. Concurrently, quinidine sulfate 0.4 Gm. should be given intramuscularly, to be followed by 0.2 Gm. every four hours day and night. The latter dose should be increased to an amount sufficient to control the rhythm and continued as a maintenance dose for about a week. Patients with first degree heart block present no serious problem, but those with second degree, or complete atrioventricular dissociation should be treated with barium chloride 32 mg. every four hours.[4] Epinephrine 0.25 cc. 1:1000 solution subcutaneously may be given either separately or in conjunction with the barium chloride. These measures are essential for the treatment or prevention of Adams-Stokes attacks.

In the event of paroxysmal atrial fibrillation, quinidine sulfate should be given as follows: an initial dose of 0.4 Gm. intramuscularly or by mouth, should be followed by four hourly doses of 0.2 Gm. with each successive dose being increased at the rate of 0.1 Gm. per dose. When the rhythm has been reverted to normal, a maintenance dose adequate to sustain the normal rhythm should be given for at least one week after reversion.[5]

It is anticipated that the findings and suggestions in these usually fatal cases of myocardial infarction may lead to the salvation of at least a few of such cases and stimulate further explorations of prognosis and treatment.

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Discussion (Abstract)

Dr. Louis F. Bishop, New York, N. Y. I would first like to congratulate Drs. McMillan and Myers for this fine study on one of the laboratory procedures that help in determining the prognosis of a patient who has had a myocardial infarction. To review the number of electrocardiograms necessary to make these observations is no small piece of work in itself. I agree (as has been quoted in their paper) that prognosis or the foretelling of the probable course of a disease, or the forecasting of the outcome of a disease by a physician who is not forced to do so is only done by a foolish physician. I have also heard that the only people that should indulge in it are the prophets themselves.

Nevertheless, it is important to recognize the seriously ill patient from the beginning of the attack because, as the authors have stated, vigilant medical care and therapy is required.

Granted that we cannot foretell the future of a patient who has had a myocardial infarction, we should try to recognize the patient who is in imminent danger. In this disease, as in no other, death may take place with great suddenness when everything seems to be going most favorably.

There has been an attempt, also, by some authors to divide the myocardial infarct patient into the "good risk" and the "poor risk" patient to decide whether anticoagulants should be given or withheld. Drs. McMillan and Myers have not mentioned this point because I believe it is their custom, as it is ours, to use anticoagulants routinely where possible.

The physician bases his prognosis on a number of factors in an individual patient—not on mass statistics—but what he sees in the single case. Some of these points have been mentioned in the paper. The age of the patient is important because mortality increases with the age of the patient. It is also important to determine whether a patient has had a previous attack, because the mortality rate is significantly higher in patients who have had a prior infarct. There is also no question that a high leukocytosis and a high temperature may mean severe injury. Intractable pain or pain with diffuse radiation is another symptom that is usually suggestive of a severe injury. Of all the clinical features of myocardial infarction that, in my own experience, may indicate a fatal prognosis, most important is cardiogenic shock. In spite of the administration of vasopressor substances mentioned by Drs. McMillan and Myers in their paper, the ultimate outlook of these patients is very bad. What is even more disconcerting is the fact that the patient may be free of pain and mentally clear and yet no pulse or blood pressure can be obtained or sustained for very long, and the prognosis is hopeless.

There is no question that abnormal rhythms alter the prognosis, but one must not be too pessimistic when confronted with an arrhythmia. I have recently seen 2 patients who had complete A-V dissociation following posterior wall infarction make a good recovery. Paroxysmal auricular fibrillation or flutter, I have not considered always of serious prognostic import. Ventricular tachycardia on the other hand, unless controlled by vigorous treatment as outlined in this paper, is nearly always a fatal complication. I have not felt that bundle branch block noted in the electrocardiogram early in myocardial infarction meant a poor prognosis. I have recently seen such an electrocardiographic picture with a good recovery.

There are several questions that I would like to ask which I think will help clarify this study. It was not clear to me what specific electrocardiographic criteria were used to decide which electrocardiograms were to be placed in the "impending death" category.

I have always felt that the S-T displacement indicated the freshness of the infarct and that an unusual degree of displacement was not of prognostic importance. I agree that some idea of the size of the infarct can be gained from the degree of electrocardiographic alterations, and when the changes are widespread, in-

volving the leads V1-V6, one can say that the infarct is large which is of prognostic significance. Serial tracings are always of importance, but in this report most of the patients did not live long enough to obtain them. My impression has been, although I cannot prove it, that a posterior wall infarct has a somewhat better outlook than an anterior one.

I would, of course, be very much interested in hearing of the correlation between the autopsy and electrocardiographic findings, if there is time in their concluding remarks, and any points in the associated laboratory data that might be of interest.

Drs. McMillan and Myers were kind enough to allow me to study the electrocardiograms shown in their slides, prior to this discussion. There are noted in the captions other points that point toward a poor prognosis, beside the electrocardiogram,—shock in one, shock and advanced age in another, extreme radiation of pain in a third, and so forth. This brings me to my final point of discussion. Studies such as this are extremely valuable and much is to be learned from them, but the physician must not base his prognosis on any single laboratory study, but on a careful appraisal of the patient from every viewpoint.

Dr. McMillan (Closing). The electrocardiographic criteria have been divided into two groups. The first group showed severe and widespread elevation of the S-T segments, occurring within one to six hours after the onset of symptoms. It is pointed out that there is reciprocal depression of the S-T segments in the area of the left ventricle not involved by the myocardial infarction. The second group in which the mortality figures were even higher was composed of patients who within a few hours after onset developed abnormalities of the cardiac rhythm as mentioned in the body of the paper. No effort was made on our part to apply exact measurement of the degree of S-T segment changes.

Our thanks are due Dr. Bishop for his complete discussion of this paper.

Fifty-third Annual Meeting of Southern Medical Association in Atlanta, Ga., November 16-19, 1959

Shoes as a Potential Hazard to Surgical and Obstetrical Patients

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Bacteria resistant to antibiotics have posed problems to hospital administrators in recent years. A serious effort is being made to trace the sources of infection. The matter of the surgeons' shoes may be one to be considered as this study shows.

IN A CASUAL CONVERSATION an air-conditioning engineer from Montreal made the statement that bacterial counts in the air of operating rooms[1,2] frequently rose when the surgeon walked into the operating room. The engineer based his observation on cultures made from bacterial filters attached to a closed-circuit air-conditioning system in a university hospital operating room. One of us (J.G.C.) when discussing the matter, suggested that the surgeons' shoes were probably one source of the air contamination.

Materials and Studies

In order to investigate this possibility 30 pairs of shoes (15 surgeons' and 15 obstetricians') from lockers in surgery and obstetrics were studied. The shoes were handled aseptically, using sterile gowns, gloves and masks, and a single sterile swab dipped in saline was stroked once across the top and another swab once across the sole and arch of one of each pair of shoes (making 60 swabs from the 30 pairs of shoes). The swabs were placed in thioglycolate broth and taken to the laboratory where they were streaked onto blood agar plates. The plates were incubated aerobically and anaerobically and examined for bacteria and fungi.

Cultures from every pair of shoes had multiple colonies. More than 70 different strains of organisms were isolated including some 23 strains of hemolytic staphylococci, 5 strains of Proteus, 1 strain of Neisseria, 50 beta-hemolytic gram-positive rods and numerous fungi. Among the 23 strains of hemolytic staphylococci, 5 were penicillin-resistant and all were coagulase negative. All the organisms isolated are ubiquitous and might be expected to be found widely in nature, especially

TABLE 1

	Aureomycin	*Bacitracin*	*Chloromycetin*	*Streptomycin*	*Erythromycin*	*Novobiocin*	*Polymyxin B*	*Magnomycin*	*Terramycin*	*Penicillin*	*Tetracycline*
Staph. 1	+	+	+	+	+	+	+	+	+	+	+
Staph. 2	—	+	+	+	+	+	+	+	—	+	—
Staph. 3	+	+	+	+	+	+	+	+	+	+	+
Staph. 4	—	+	+	+	+	+	+	+	—	+	—
Staph. 5	+	+	+	+	+	+	+	+	+	+	—
Proteus 6	+	+	+	+	+	+	+	+	+	+	+
Staph. 7	+	+	+	+	+	+	+	+	+	+	+
Staph. 8	+	+	+	+	+	+	+	+	+	+	—
Staph. 9	+	+	+	+	+	+	+	+	+	+	+
Staph. 10	+	+	+	+	+	+	+	—	+	—	+
Staph. 11	+	+	+	+	+	+	+	+	+	+	+
Staph. 12	+	+	+	+	+	+	+	+	+	+	+
Staph. 13	+	+	+	+	+	+	+	+	+	+	+
Proteus 14	+	+	+	+	+	+	+	+	+	+	+
Staph. 15	+	+	+	+	+	+	+	+	+	+	+
Staph. 16	+	+	+	—	+	+	+	+	+	—	+
Proteus 17	+	+	+	—	+	+	+	+	+	+	+
Staph. 18	+	+	+	+	+	+	+	+	+	+	+
Staph. 19	+	+	+	+	+	+	+	+	+	+	+
Staph. 20	—	+	+	—	+	+	+	+	—	+	—
Staph. 21	+	+	+	+	+	+	+	+	+	—	+
Staph. 22	+	+	+	+	+	+	+	+	—	—	—
Proteus 23	+	+	+	+	+	+	+	+	+	+	+
Staph. 24	+	+	+	+	+	+	+	+	—	—	—
Staph. 25	+	+	+	+	+	+	+	+	+	+	+
Proteus 26	+	+	+	+	+	+	+	+	+	—	+
Staph. 27	+	+	+	—	—	+	+	+	+	+	+
Staph. 28	+	+	+	+	+	+	+	+	+	+	+

+Sensitivity
—Cross-resistant

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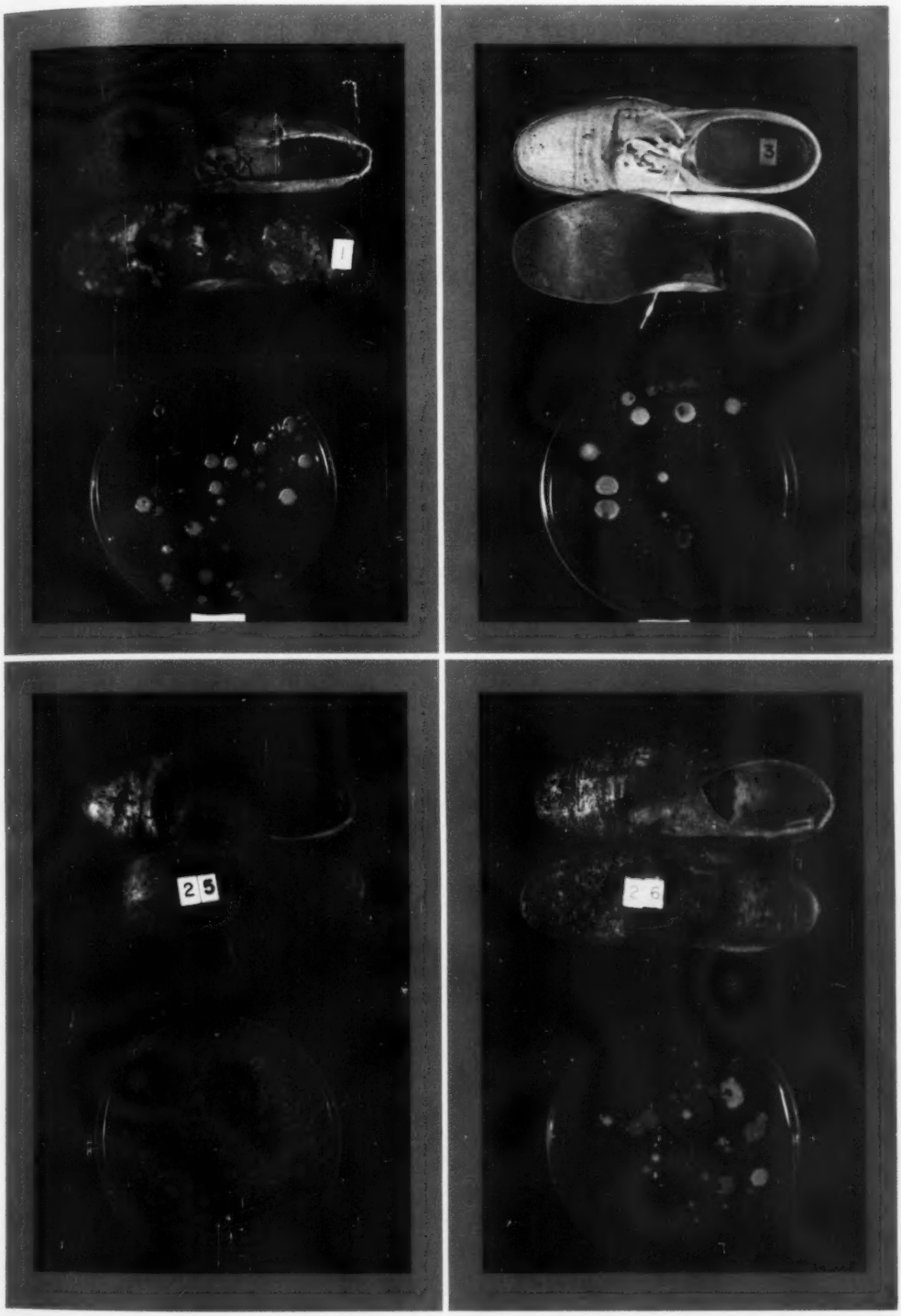
1
3
25
26

in areas of constant human habitation. The fact that the hemolytic staphylococci were all coagulase negative does not negate the possibility of their pathogenicity, but merely indicates that they have not immediately been associated with an acute or fulminating human infection.

Laboratory strains of staphylococci, coagulase positive on primary isolation from clinical specimens often become coagulase negative on repeated subculture. The antibiotic resistance of these organisms indicate that they were lately associated with clinical infections treated with antibiotics during which resistance developed. This antibiotic resistance, in addition to indicating past pathogenicity, predicts the possibility of difficult and perplexing therapeutic problems should these organisms regain entry into susceptible human hosts (Table 1). It will be noted that organisms Nos. 10, 16, 21, 22, 24 and 26 are penicillin-resistant. The organisms of greatest hazard are No. 16 which is resistant to penicillin and streptomycin. Nos. 22 and 24 which are resistant to penicillin, tetracycline and terramycin and No. 20 which is resistant to streptomycin and several tetracyclines.

Discussion

The shoes varied from those covered with old blood, pus, amniotic fluid, and mucus, to some which were reasonably clean. Most were in a bad state of repair. Years ago it was recognized that there was a serious danger in the use of shoes worn in from the street to the operating and delivery suites. A solution was attempted in many hospitals when surgeons and obstetricians purchased special shoes not to be removed from the respective delivery and operating room suites. At the present time in most hospitals in Alabama and neighboring states each surgeon and obstetrician has a special pair of shoes which is used solely for wear in the surgery or delivery room. The shoes are generally unsterilized and often in various degrees of uncleanliness. With the reduction in humidity from air-conditioning, colonies of bacteria on such shoes may very well be thrown into the air and circulated in the operating or delivery suites (spray from infected material at operation may be carried throughout the hospital if the air-conditioning units in the surgery and delivery rooms are on the same circuit as that for the entire hospital). In fact another source of contamination might be air from other parts of the hospital brought into the operating, delivery and nursery suites.

Cultures of the throats of the personnel (nurse, orderlies, anesthestists, etc.) in the operating and delivery suites of one hospital indicated that 40% carried hemolytic staphylococci or some other pathogen. Perhaps a gargle with saline solution or mucus-removing detergent twice daily by all persons entering the operating, nursery or delivery suites would be helpful.

It is believed that shoes which could be placed in a washing machine at the end of an operation or delivery would greatly reduce the bacterial flora on the shoes. Such shoes are available and could perhaps be equipped with a rust-proof metal grounding attachment. A temporary expedient would be the well-known cloth shoe covers tied about the instep. This simple expedient, though not a complete solution, might greatly reduce the present potential shoe-hazard in obstetrics and surgery. Ultraviolet sterilization equipment might be installed in the locker rooms of all hospitals.

Summary

Fifteen pairs of obstetricians' and 15 pairs of surgeons' shoes were photographed and cultured. These shoes were used only in the respective air-conditioned suites. A fertile reservoir of pathogens was encountered, 80% of the shoes having hemolytic staphylococci, Proteus or other pathogens. Many were antibiotic-resistant. Cloth shoe covers in pediatric, obstetric and surgical areas would be an improvement. Special washable conductance shoes, frequent cleaning of bacterial filters on air-conditioning units in such suites, and measures to reduce the nose and throat pathogens among personnel in the operating theater are suggested.

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The following two papers consider the problem of resistant staphylococcal infection in infants and young children. The strains of this organism which have become resistant to the common antibiotics are carried in the nasal passages especially of hospital personnel. In the nurseries for the newborn infections with such organisms may become epidemic, manifested as infections of the skin, subcutaneous tissues, lungs and/or blood stream. Many end fatally. Not infrequently the infections manifest themselves after the child has been discharged from the hospital. Strict aseptic technics, screening of personnel for carrier-states, and cleanliness in the hospital are the major prophylactic measures. The newer, albeit more toxic antibiotics, are the more successful in combating the infections with resistant staphylococci.

Management of an Outbreak of Staphylococcal Infection in a Nursery for the Newborn and the Results of an Intensive Control Program*

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STAPHYLOCOCCAL INFECTION has been a problem for practicing physicians for many years. Occasionally, this matter would become acute when severe infections such as osteomyelitis occurred or when purulent complications appeared in unrelated disease processes. The advent of chemotherapeutic and antibiotic agents at first served to minimize the role of the staphylococci as important pathogenic organisms. As a result of this, basic research concerning the staphylococcus was in large part discontinued. Unfortunately, this organism has been slowly, but surely, acquiring "special biologic characteristics" which have pushed it into the forefront as an important factor to be dealt with when a patient is admitted to a hospital.[1] Certain strains of *Staphylococcus aureus* are now known to be the cause of outbreaks of severe infections in hospitalized patients. Blair and Carr[2] in the United States, and Bynoe, Elder and Contois[3] in Canada, published the results of studies on the bacteriophage typing of many strains of staphylococci isolated from hospital infections. Evidence rapidly accumulated to show that these strains were similar to those causing hospital infections in other parts of the world.[4,5] One of the most distressing developments of the problem of infections with these organisms has been the occurrence of epidemics in nurseries for the newborn. Shaffer and associates[6] pointed to the problem as it could exist in such nurseries and gave specific recommendations for the control of these infections. Shortly before this paper appeared in the literature it became apparent that what "couldn't happen to us" had already happened and, in fact, was well upon us. The present paper consists of a chronologic report of this outbreak at the University of Texas Medical Branch Hospitals and the results of a strenuous control program over a two year period.

Bacteriologic and Clinical Studies

In the fall of 1956 the physicians in the outpatient department began to note that babies in the neonatal age group who had been delivered on the obstetrical service were presenting with severe skin infections, and for the first time in several years babies with mastitis were being seen. This warning of impending danger, which is often the first sign of trouble, was not regarded very seri-

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ously at the time the first infected babies appeared, but as the number of cases rapidly increased it became apparent that a common factor must be involved. By the end of October there had accumulated 40 cases of severe pyoderma and mastitis. During this time there had been no reports of mastitis or other infection in the mothers of these infants. The situation became so serious that it was suspected these infections must have been the result of the stay in the nursery for the newborn. Therefore, plans were made for a survey of the nurseries to determine whether there was a specific etiologic agent, and if so, its source and distribution in the nursery environment and personnei.

On October 31, a bacteriologic survey of all personnel on the obstetrical service and in the nursery areas was carried out. Cultures were taken from the nasopharyngeal areas and were examined for *Staph. aureus.* All isolates of this organism were tested for antibiotic sensitivity and subsequently were phage-typed. Eight persons who were discovered to have positive cultures for *Staph. aureus* were asked to take a 5 day leave of absence from their duties and to undergo systemic therapy with erythromycin, to which the organisms were sensitive *in vitro.* All infants were cultured on November 1, and 10 infants were found to have positive cultures. These cultures were studied as above.

At this time, phage-typing facilities were set up by Dr. Warren R. Stinebring, who obtained the necessary materials through the courtesy of Dr. John E. Blair. It was found that of 13 cultures from earlier infections, 11 were phage-type 42B/44A/81. (This has subsequently been designated the "80/81" strain.) Of the eight personnel who have been found to harbor *Staph. aureus* in their nasopharynx, one was found to be a carrier of this strain at this time while 7 of 10 *Staph. aureus* isolates from 23 newborns were of the same pattern.

All of the nursery procedures were reviewed and it was decided that a great many factors in our environmental situation must be remedied. The two nurseries, one for colored infants and one for white, were closed to further admissions on November 3 and a composite nursery in a clean area was established. Plans were made for thorough cleaning of the original nursery areas to take place as soon as the last baby was discharged. Certain structural changes were made in order to provide mechanical barriers between the nursing station and the cubicles for infant care. Traffic through the nursery corridors was reduced to a minimum. A regular cleaning schedule was instituted so that the complete general housecleaning which was carried out in the original nursery areas could be continued. Care of the laundry was considered and the method of handling the nursery supplies was changed. All nursery personnel were given special instruction in proper handwashing and other nursery technics.

It was decided that hereafter cultures should be taken from the anterior nares, since this has been established as the most frequent site of colonization.[7] Cultures were obtained from the regular nursery personnel once a week and personnel to be assigned to this area were screened prior to the beginning of their duties. For a period of five months cultures were taken from all mothers and infants on the day of discharge from the hospital. During the first four months erythromycin in therapeutic doses was ordered for all infants admitted to the nursery, to be administered throughout their hospital stay. pHisohex bathing was included as a part of the nursery care, following the recommendations of Shaffer and associates.[6]

On November 21 the original nursery areas were ready for occupation. The staffing was arranged in such a manner that no one having a nasal culture positive for *Staph. aureus* phage-type 80/81 was permitted on duty in the nursery. This policy was enforced for a period of 19 months, during which time no serious staphylococcal infection occurred in any baby, either during his hospital stay or after discharge. The occasional appearance of a minimal pustule which yielded a culture positive for the epidemic strain was noted during the later months of this control period. Periodic surveys of the anterior nasal areas of the infants in the nursery, taken at the time pustules were reported, revealed only an occasional infant with a positive phage 80/81 culture. These infants were all given local antibiotic nasal treatment and after discharge were followed in the outpatient department.

During the very early phase of the above control program 8 cases of staphylococcal pneumonia were admitted to the pediatric

service. All occurred in infants who had been delivered during August, September and early October on the obstetrical service of this hospital, prior to the establishment of the prophylactic regimen with erythromycin. There were two deaths among these babies.

In January of 1957, there was evidence that the epidemic strain was present on some of the other hospital services. A hospital-wide survey was conducted[8] to determine the number of patients and personnel who were harboring this strain in their anterior nares. Carriers were given a course of treatment consisting of nasal application of nonsystemic antibiotic ointment. However, further control measures on personnel in areas other than on the newborn units were discontinued shortly thereafter.

Control Measures

In the Fall of 1957, there was a severe outbreak of staphylococcal disease on the Medical Service. Early in January, 1958, a nurse who had been caring for some of the adult patients developed fatal staphylococcal sepsis. This, coupled with the increased incidence of staphylococcal infection on the adult wards, precipitated the establishment of a Surveillance Committee appointed by the hospital Chief of Staff. This committee began to function early in February and by the end of the month had, with the cooperation of the Director of Hospitals, established an adult isolation unit of 18 beds, a central area for the carrier control program, and for the consistent medical care of all hospital personnel having lesions. Personnel with lesions were removed from duty in areas where there were patients. Nasal staphylococcus carriers were placed on nonsystemic nasal antibiotic ointment or spray. These preparations were used three times a day during the work week, and discontinued for two days. Following this rest period cultures were again taken. Treatment was continued until a negative report was obtained. In the large majority, negative cultures followed one course of treatment, with approximately 85% being cleared by one or two courses of treatment.[9]

A set of rules and regulations to be followed throughout the hospital was prepared. These were published as an inclusion in a paper by Mudd.[10] It was not necessary to revise the nursery routines to fit into these directives. Although it was impossible to institute all of the recommendations immediately, a review of the hospital after seven months shows that most of these are now in force.

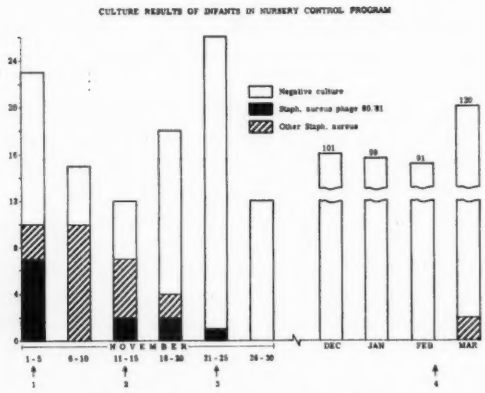
At the end of May, 1958, the directors of the nursing service informed the Surveillance Committee that, because of shortage of personnel it would no longer be possible to eliminate carriers from the nursery area. A compromise was made whereby positive carriers worked in the nursery with rigid supervision while under local nasal treatment. The personnel shortage continued to be very acute through the month of June. During this month 6 cases of minimal pyoderma caused by phage-type 80/81 organisms developed in nursery infants. Early in July there was one case of severe pyoderma and one case of mastitis, the first seen since November, 1956. Later in the summer another case of severe pyoderma was admitted to the hospital and the second case of mastitis occurred. In August, 2 cases of staphylococcal pneumonia were admitted to the Pediatric Service. All of the infants involved had been delivered here. Although 3 of these severe cases were due to 80/81 strains, there were no deaths from these infections.

The delivery rate in this hospital increased abruptly between July and August of 1958. At the end of August and early in September the nursery area was extremley overcrowded. At the time when there were 6 infants with pustules in the so-called isolation unit of the nursery suite, the Surveillance Committee ordered a review of the nursery situation. It was strongly recommended that the nasal carriers again be removed from duty and that the population of the nursery be reduced to a "sensible level." Because of the increase in infection it was also decided to institute prophylactic medication during the infants' hospital stay. This time novobiocin was used. Following general housecleaning of the nursery areas and the tightening up of all control measures there has been a complete cessation of any type of infection in the nursery. It is to be hoped that there will be no delayed cases of pneumonia resulting from this episode.

Results

The data concerned with the incidence of any *Staph. aureus* in infants for a five month

FIG. 1



(1) Week of initial culture survey and establishment of composite nursery. (2) Institution of erythromycin prophylactic therapy. (3) Last positive infant nasal culture 80/81 strain. (4) Erythromycin prophylactic therapy discontinued.

period is presented graphically in figure 1. A total of 99 cultures were taken from the nasopharyngeal areas, in determining the strain responsible for this epidemic. Following this first group of cultures all specimens were obtained from the anterior nares.. In table 1 it is shown that *Staph. aureus* was found in 10 of 23 babies during the first week of the study. Subsequent phage-typing placed 7 of these in the group 80/81. These organisms were resistant to penicillin, tetracycline, and streptomycin, and sensitive to erythromycin, novobiocin, chloramphenicol, neomycin and bacitracin. The last infant's nasal culture positive for *Staph. aureus* was reported in the final week of November, there being no other positive cultures until the beginning of March. At this time two cultures of staphylococci not of the epidemic type were reported. At the

TABLE 1

CULTURE RESULTS OF INFANTS IN THE NURSERY CONTROL PROGRAM

Date	*Total*	*Negative*	*Staph. aureus*	*Phage 80/81*
November				
1-5	23	13	10	7
6-10	15	5	10	0
11-15	12	3	9	2
16-20	18	14	4	2
21-25	26	25	1	1
26-30	12	12	0	0
Total	106	72	34	12
December	101	101	0	0
January	99	99	0	0
February	91	91	0	0
March	120	118	2	0

TABLE 2

CULTURE RESULTS OF PERSONNEL IN THE NURSERY CONTROL PROGRAM

	Number of Cultures	*Staph. aureus Phage 80/81*
Initial Survey	99	1
November		
11-15	68	4
16-20	27	5
21-25	19	1
26-30	67	5
Total	280	14
December	82	8
January	107	5
February	87	0
March	71	0

end of February the outbreak appeared to be under control and erythromycin was discontinued at this time. Regular culturing of infants and mothers was continued for another month. The results of the personnel cultures during the intensive study and stabilization period are shown in table 2.

Table 3 shows the status of cultures from the mothers and their babies at the time of discharge from the hospital. Because of the potential danger of nasal colonization without apparent infection, it was felt that this information might be helpful should any trouble be noted after leaving the hospital. The consistent occurrence of nonepidemic coagulase positive staphylococci in the mothers' nasal cultures represents normal flora.

TABLE 3

CULTURE RESULTS OF MOTHERS AND INFANTS AT DISCHARGE NOVEMBER 14, 1956 THROUGH APRIL 1, 1957

Date (Weeks)	*Total*		*Negative*		*S. aureus*		*Phage 80/81*	
	M	*I*	*M*	*I*	*M*	*I*	*M*	*I*
11/9 - 11/16	28	30	13	11	15	19	1	3
11/17 - 11/24	29	29	20	27	9	2	1	1
11/25 - 12/2	35	34	25	34	10	0	0	0
12/3 - 12/10	20	21	17	21	3	0	0	0
12/11 - 12/18	33	34	28	34	5	0	0	0
12/19 - 12/26	17	18	12	18	5	0	0	0
12/27 - 1/3	20	20	17	20	3	0	0	0
1/4 - 1/14	26	26	22	26	4	0	0	0
1/15 - 1/30	64	64	55	64	9	0	1	0
1/31 - 2/13	39	40	29	40	10	0	0	0
2/14 - 2/28	47	47	41	47	6	0	0	0
3/1 - 3/15	57	59	51	57	6	2	0	0
3/16 - 4/1	55	56	48	56	7	0	0	0

During the fall of 1957, when the number of staphylococcal infections was increasing throughout the hospital, student nurses, medical students and resident staff had to be denied duty in the nurseries with increasing frequency because they had become carriers of epidemic staphylococci. It was necessary to make many changes in the assignment schedules of students and residents to maintain the rigid rules that had been set concerning carriers.

In the period following the suspension of erythromycin prophylaxis, and extending through May, 1958, a few minimal pustules were reported from the newborn nursery. Nasal culture surveys of all infants in the nursery at these times showed only an occasional culture positive for *Staph. aureus*. As with the infants, an occasional person on duty in the nursery was found to be carrying the epidemic strain. None of these carriers ever developed lesions, and all responded to treatment.

However, during June, July and August of this year, due to turnover in personnel and vacation schedules, the staffing problem in the nurseries became desperate. This combined with an abnormally high seasonal rise in delivery rate, resulted in a deterioration of the control program in the area for the newborn. For the first time, personnel who had previously been consistently negative became carriers. Four of these developed lesions, the first seen in nursery personnel.

Discussion

This diary of events has been documented in order to demonstrate the characteristics of epidemic staphylococcal infections in newborns as they can occur in a general hospital. The beginning of trouble may often pass unnoticed since, although nasal colonization occurs in the hospital, the resulting infections may not appear for some time after discharge. As a matter of fact, in our experience the cases of pneumonia reported did not occur until two and one-half to four months after dismissal from the nursery.

The responsibility of determining the causative agent and its distribution throughout the hospital and of establishing measures for the control of an outbreak even in a limited segment of a general hospital presents many problems. Much literature on staphylococcal cross-infection has appeared within the past several years, but emphasis on the epidemic nature of these infections was at first directed primarily toward the problem as seen by pediatricians, obstetricians and surgeons. The relatively mild nature of most staphylococcal infections in adults has made it difficult to establish in the mind of medical and administrative staffs of hospitals the importance of epidemic strains as potentially dangerous pathogens in a general hospital population. The feeling that often exists is that if a department is confronted with such a problem, it should be handled and solved by that department alone. Although this "head in the sand" attitude has not led to direct resistance to control measures, the negative attitude of some key personnel has made the implementation extremely difficult. On the other hand, a satisfying aspect has been the wholehearted cooperation and efforts of personnel in actual charge of the intimate care of the patient, i.e., professional nurses, the resident and intern staff and the higher class of nonprofessional aides. The supervisors of key service departments, particularly housekeeping, immediately recognized the potential danger and provided excellent cooperation in establishing and maintaining control measures.

One of the major problems of a surveillance committee is to maintain the interest and cooperation associated with the original momentum once the emergency nature of a situation has subsided. A carefully planned in-service training program should be established, and periodic reports made to all responsible personnel.

The reappearance of infections on the service for the newborn after a compromise in the control measures, established the interrelation of all other hospital areas and operations with the nursery service. Even though the infants represent a large percentage of the more susceptible hospital population, the same problems exist wherever critically ill or debilitated patients must be cared for. Therefore, it would seem that staphylococcal epidemics should cease to be considered a primary concern only of nursery areas.

Summary

1. An outbreak of staphylococcal infection in the nursery area of a university teaching hospital has been described. The laboratory

methods used to establish the etiologic agent have been discussed in detail.

2. The control measures which prevented any serious staphylococcal infection for a period of 19 months have been noted.

3. The importance of the role of healthy nasal carriers was emphasized.

4. The interrelationship of all other hospital areas and operations with the nursery service was considered to be of utmost importance in any control program.

Acknowledgment

The active participation of Dr. Warren R. Stinebring and Dr. Ray H. Redmond in the initial phases of this program is gratefully acknowledged. The success of this program has in large part been due to the close collaboration among the supervisors of the Obstetrical and Nursery Services with the Executive Director of Housekeeping Services. The authors are also grateful to Miss Jo Ann Holzman for her technical assistance.

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The Antibiotic Management of Staphylococcal Disease in Infants and Children*

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THE IMPORTANCE OF PROGRAMS for the prevention of staphylococcal disease is well recognized.[1] Until the aims of prevention can be realized, however, it is of value to review methods of management applicable to the patient presenting with this disease. Variations in the disease and its causative organism[2] necessitate the clinical evaluation of new antistaphylococcal antibiotics and reappraisal of the older agents which have been effective against the staphylococcus during the last decade.

The following article presents an analysis of antibiotic management of 204 cases of staphylococcal disease in infants and children seen at Jefferson Davis Hospital from 1956 to 1958. The broad principles of management of these patients are discussed in another paper.[3]

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Description of Cases

Selection. The cases selected for study were limited to those occurring in a time interval (1956-1958) during which the phage-types and antibiotic sensitivities of prevalent strains at Jefferson Davis Hospital were comparable. Only those cases in which the diagnosis was established by identification of the organism and in which there was a minimal follow-up period of one month were included.

Age distribution. The ages of the patients ranged from 12 hours to 12 years. There were 155 babies under 2 months of age, 32 babies

TABLE 1

AGE DISTRIBUTION OF 204 CASES OF STAPHYLOCOCCAL DISEASE IN INFANTS AND CHILDREN

Age	*Number*
Newborn	155
2 months—2 years	32
Older children	17
Total	204

from 2 months to 2 years of age, and 17 older children (Table 1).

Site of disease. The forms of disease encountered are shown in table 2. Sixty-six patients had superficial infections such as impetigo and conjunctivitis. The other 138 had more serious involvement. Fifty-seven of this 138 had involvement of more than one organ system. Fifty per cent of the newborn infants (both premature and newborn) had disseminated infections. After the age of 2 months the percentage of patients with multiple sites of involvement dropped to approximately 25% (Table 3).

Description of the organisms. Eighty per cent of the staphylococcal infections in this group of patients were classified as hospital-acquired, and 20% were considered to be of extra-hospital origin. All of the strains were tested for antibiotic susceptibility by the disk and tube dilution technics. The predominant "hospital strain" was a strain which was resistant to penicillin, streptomycin, tetracycline, and erythromycin. Fifteen per cent of the "street" strains were resistant to penicillin, 25% to streptomycin, 3% to tetracycline, and none to erythromycin. Ninety-five per cent of the strains, both nosocomial and from extra-hospital sources, were susceptible to novobiocin and bacitracin and 100% were

TABLE 2

MAJOR SITE OF INFECTION AND MORTALITY RATE IN 204 CHILDREN WITH STAPHYLOCOCCAL DISEASE

Site	*Number*	*Deaths*	*Percentage Mortality*
Impetigo neonatorum	56	0	0
Septicemia	40	19	47
Pneumonia	26	5	19
Deep subcutaneous abscess	36	3	8
Gastroenteritis	16	2	12
Conjunctivitis	10	0	0
Meningitis	3	2	67
Miscellaneous	17	2	12
Total	204	33	11

TABLE 3

RELATIONSHIP OF DISSEMINATION AND MORTALITY RATE OF STAPHYLOCOCCAL DISEASE TO AGE OF PATIENTS

Age	*Number*	*Disseminated Disease*	*Mortality*
Premature	23	51%	43%
Full-term	66	50%	26%
2 months—2 years	32	25%	21%
Older children	17	23%	12%

susceptible to neomycin. Approximately one-half of the strains were tested against kanamycin and vancomycin. All were sensitive to these two antibiotics.

Phage-typing performed on 75% of the strains showed the predominant strain in children of all ages at Jefferson Davis Hospital to be phage-type 42B/81/44A/70. The ratio of this phage-type to other phage-types was especially high in the newborn age group. This was considered to be due not to any predilection of phage-type 81 for this age group but a reflection of the fact that the infections in the newborn were hospital-acquired.

Diagnostic methods. Extreme care was exercised in proving the etiologic role of the staphylococcus in the production of disease in these patients. The causative organism was identified by culture in each case. Emphasis was placed upon the use of the direct smear in examination of exudates and fecal material to provide a rough quantitative estimate of the relative numbers of staphylococci in comparison to other bacterial flora which might be present. Broth and pour-plate cultures were used in the diagnosis of septicemia. Differential media was employed when indicated. The diagnostic criteria are discussed in detail in a subsequent paper.[3]

Management with Antibiotics

Selection of antimicrobial agents. As many workers have pointed out, the staphylococcus is an organism whose susceptibility to antibiotics varies from strain to strain.[4,5] Therefore the first 24 to 48 hours of antibiotic therapy is of necessity empirical. The antibiotic agent or agents employed must be selected on the basis of probability of response until the results of *in vitro* testing are available. For this reason and because of the serious nature of the illnesses encountered peni-

cillin, the tetracyclines, and streptomycin were not used alone initially in any of these patients. However, when the etiologic agent proved to be susceptible to penicillin, penicillin was considered to be the drug of choice. During the first year of this study most of the patients with hospital-acquired infections were treated with a combination of erythromycin and streptomycin, erythromycin and chloramphenicol, or chloramphenicol or novobiocin alone. Disappointing results using these commonly used antibiotics and increasing awareness that a large proportion of these cases were due to the virulent phage-type 81 staphylococcus led to a trial of other antibiotics. Bacitracin and later the new antibiotic, kanamycin, were used. Both of these drugs seemed especially suitable for use in infants and children because of their bactericidal activity and because they could be administered by the intramuscular route.

The dose of the various antibiotics used is outlined in table 4. In seriously ill patients all antibiotics were given initially by the parenteral route for a minimal period of 48 hours. Oral therapy was used when the patient began to improve and where it was practical. Local antibiotic administration was used in certain types of localized infections i.e., empyema, purulent pericarditis, meningitis, and septic arthritis.

Methods of management. Since the choice of the type of medical or surgical management depends so largely on the major area of involvement, the specific methods of management are discussed by the major site of disease.

Impetigo. Fifty-six infants had impetigo alone (Table 2). In this group 36 were treated with chloramphenicol, orally or intramuscularly, 10 received kanamycin intramuscularly, and 10 were treated locally. All survived. Twenty-nine additional babies had impetigo either preceding or occurring simultaneously with more severe forms of staphylococcal disease. Fourteen of the 29 gave a history of pyoderma as the initial manifestation. Two-thirds of the 14 received systemic therapy (chloramphenicol or kanamycin) and one-third received local treatment. Systemic antibiotic therapy was used in the majority of the patients with impetigo because of the highly invasive nature of the etiologic agent with which we were dealing. This group of patients is too small to permit a decision whether or not the use of systemic therapy influenced systemic invasion. At the present time there are no controlled data available on the safest method of treating impetigo neonatorum due to epidemic strain "81."

Conjunctivitis. Ten patients were treated for staphylococcal conjunctivitis (Table 2). Four patients received systemic antibiotics and 6 received local therapy alone. Response was uniformly good with no marked difference in the duration of infection in the two groups. The average length of treatment was one week.

TABLE 4

DOSAGE AND ROUTES OF ADMINISTRATION OF ANTISTAPHYLOCOCCAL ANTIBIOTICS USED IN 204 PATIENTS WITH STAPHYLOCOCCAL DISEASE

Drug	*Route*	*Daily Dosage (mg./Kg.)*	*Intervals*
Tetracycline	Oral	30- 50	6 hrs.
	I. M.	30- 50	
	I. V.	30- 50	
Chloramphenicol	Oral	30-100	6 hrs.
	I. M.	30-100	6-12 hrs.
	I. V.	30- 80	
Erythromycin	Oral	20- 50	6 hrs.
Novobiocin	Oral	20- 50	6 hrs.
	I.V.	20- 30	
Streptomycin	I. M.	20- 50	8 hrs.
Kanamycin	I. M.	10- 50	6-12 hrs.
	Topical	2.5 mg./ml.	
Penicillin G (Aqueous)	I. M.	20,000-50,000 U/Kg./day	3-6 hrs. or
	I. V.	20,000-50,000 U/Kg./day	continuous I. V.
Bacitracin	I. M.	600- 1,200 U/Kg./day	6 hrs.
	Topical	500 U/ml.	

Subcutaneous abscess. The group of 36 patients having deep subcutaneous abscess as the major site of infection was comprised of 25 newborn babies with breast abscesses or deep subcutaneous abscesses in other sites, and 11 older infants and children with deep subcutaneous abscesses. Incision and drainage of the abscess was performed in three-fourths of the cases. The others had resolution of the process during administration of antibiotics. Twenty-nine of the 36 children were treated with bacteriostatic agents, the majority receiving erythromycin and chloramphenicol or novobiocin, or with a bacteriostatic agent in addition to penicillin or streptomycin (Table 5). In this group 3 patients expired, all of whom were newborns. In 2 of the 3, adequate drainage of the initial staphylococcal lesion was obtained but a superimposed infection due to *Pseudomonas aeruginosa* occurred and the terminal cause of death appeared to be pseudomonas septicemia. In the third case the area of cellulitis resolved, but dissemination and secondary staphylococcal involvement of the lungs developed while the baby was under treatment. Seven patients, 4 newborns and 3 older infants, were treated with a single bactericidal agent, kanamycin (Table 6). In four cases drainage was required for abscess formation and 3 resolved under therapy. There were no deaths on this regimen.

Not only was the mortality rate higher in the newborn period than in older infants and children, but the morbidity was greater in this age group. The average duration of therapy was two weeks.

Septicemia. Forty patients proved to have staphylococcal septicemia (Table 2). This included 31 babies less than 2 months of age, 4 in the 2 months to 2 years group and 5 in older children. Twelve children were treated with a bacteriostatic agent (erythromycin, chloramphenicol, novobiocin) alone, in combination with another bacteriostatic agent, or in combination with penicillin or streptomycin (Table 5). Eight of these children died. Eight children received bacitracin initially or bacitracin late after failure of response to bacteriostatic agents (Table 6 and Fig. 1). There were 3 deaths in this group. Kanamycin was used in the treatment of 16 patients with 4 deaths (Table 6). Another 4 children died within twenty-four hours of admission so the drug was considered to have had an inadequate trial. Surprisingly, in the patients with septicemia, the percentage of deaths was not greatest in the newborn age group. Fourteen of the 31 newborns, 4 of the older infants, and one 4 year old girl died. Analysis of these unexpected figures revealed that each of the older infants was critically ill on admission, with a history of illness of 6-10 days duration with therapy. The 4 year old girl had a blood stream invasion secondary to staphylococcal infection of an 80% second and third degree body burn. Her death was probably due principally to the severity of the burn.

The optimal duration of treatment was difficult to determine. Although the temperature course, white blood count, and differential were not helpful in every case they served as a guide in many cases. Increase in appetite and weight gain were very reliable guides in the young infant. Because of the high relapse rate the average duration of therapy for septi-

TABLE 5

RESULTS IN THE TREATMENT OF 73 CASES OF SERIOUS STAPHYLOCOCCAL DISEASE USING BACTERIOSTATIC ANTISTAPHYLOCOCCAL ANTIBIOTICS*

Site of Infection	*Number*	*Recovered*	*Died*	*Percentage Mortality*
Deep subcutaneous abscess	29	26	3	10
Septicemia	12	4	8	67
Pneumonia	17	2**	2	11
Gastroenteritis	8	6	2	25
Miscellaneous	7	6	1	14
Total	73	44	16	22

*Bacteriostatic antibiotics used were erythromycin, chloramphenicol, novobiocin, and tetracycline.
**Fifteen patients failed to respond to initial bacteriostatic therapy and were subsequently treated with bactericidal agents.

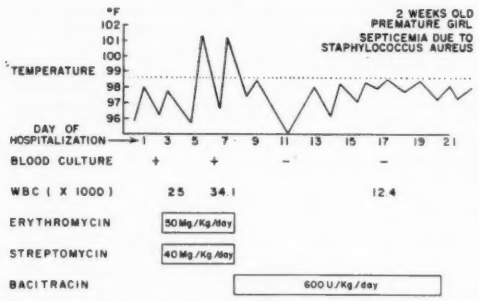
TABLE 6

RESULTS IN THE TREATMENT OF 69 CASES OF SERIOUS STAPHYLOCOCCAL DISEASE USING BACTERICIDAL ANTIBIOTICS*

Site of Infection	*Number*	*Recovered*	*Died*	*Percentage Mortality*
Deep subcutaneous abscess	7	7	0	0
Septicemia	24	17	7	29
Pneumonia	20**	19	1	5
Gastroenteritis	8	8	0	0
Miscellaneous	10	9	1	10
Total	69	60	9	13

*Bactericidal antibiotics used were bacitracin and kanamycin.
**Thirteen of the 20 patients had failed to respond to bacteriostatic therapy prior to receiving a bactericidal agent.

FIG. 1



cemia without known localization of organisms in other sites was three to four weeks.

Pneumonia. There were 26 patients with staphylococcal pneumonia. The majority of these children were between 2 months and 2 years of age. Seventeen of the children were treated initially with a bacteriostatic agent or a bacteriostatic agent in combination with penicillin or streptomycin (Table 5). Only 2 patients recovered on this therapy, 2 died and 13 subsequently responded to treatment with either kanamycin or bacitracin (Table 6 and Fig. 2). Six patients received bacitracin alone or in combination with a bacteriostatic agent; 5 recovered and one died. Kanamycin was used alone successfully in one of the cases of pneumonia. Two of the infants with pneumonia developed a fulminating infection at home and were hospitalized such a short time before death that effectiveness of the therapy could not be assessed. The age of the patient seemed to be a major factor influencing the outcome of the disease. The percentage of deaths was 30% in the neonatal period and 16% in the children from 2 months to 2 years of age. The only older child with staphylococcal pneumonia had an uneventful recovery. The minimal length of therapy was fixed at 21 days on the basis of the findings of Disney and his associates.[6]

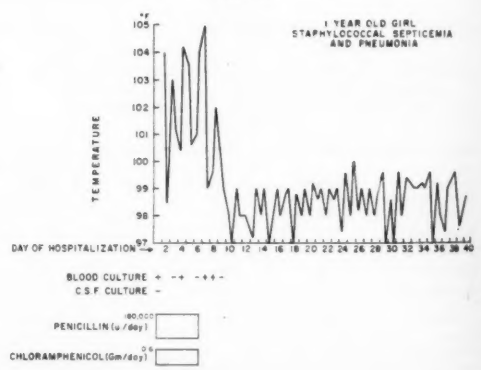
Gastroenteritis. Sixteen patients were treated for staphylococcal gastroenteritis (Table 2). The age range of these patients was 1 to 41 days. There were 2 deaths, one in a premature infant and one in a full term baby. Eight patients received a bacteriostatic antibiotic (Table 5), 6 kanamycin (Table 6), and 2 oral neomycin (Table 6). Both deaths occurred in the former group. Duration of treatment was individualized but the average length of antibiotic administration was 14 days.

Meningitis. Three patients presented with meningitis as the major difficulty. All three were under 2 months of age and had nosocomial infections. Various combinations of bacteriostatic and bactericidal drugs by intramuscular, intravenous, intrathecal, and intraventricular route were administered. In spite of vigorous therapy only one patient survived. It was possible to sterilize the spinal fluid of another of the babies but a large walled off abscess in the frontal lobe was discovered at postmortem examination. The third infant developed hydrocephalus and expired.

Miscellaneous. The seventeen patients classified as miscellaneous in table 2 had the following types of involvement: osteomyelitis 5, omphalitis 3, otitis media 3, appendiceal abscess 2, retroperitoneal abscess 1, laryngotracheobronchitis 1, ethmoiditis 1, liver abscess one. The patients with liver abscess and tracheobronchitis expired. The remaining 15 patients in this group responded to combined medical and surgical treatment. Response to kanamycin or bacitracin therapy after lack of response to chloramphenicol, erythromycin or novobiocin was striking in several instances.

Results. The results of treatment have been discussed under each entity. In summary, all of the patients with conjunctivitis and impetigo alone recovered, 105 of the more seriously ill patients recovered, 33 died—an over-all mortality of 11 per cent (Table 2). The greatest percentage of deaths was in the premature

FIG. 2



age group (Table 3), and in patients with the diagnosis of septicemia (Table 2).

In the evaluation of the antimicrobial therapy of staphylococcal infections certain factors must be considered,—the age and condition of the host, the type of surgical drainage employed, and the supportive therapy used. There seemed to be no marked difference in the distribution of these variables among the patients who received bacteriostatic agents and those who received kanamycin or bacitracin. Results, however, were significantly different in these two groups. The mortality rate in all types of patients treated with bacteriostatic drugs or bacteriostatic drugs in combination with penicillin or streptomycin was 22 per cent (Table 5). The mortality rate in patients treated with kanamycin or bacitracin alone or in combination with a bacteriostatic drug was 13 per cent (Table 6). This difference is even more striking when it is considered that in many cases kanamycin and bacitracin were not used until the pathologic process had progressed during other treatment and the patient had become critically ill.

Toxicity. Untoward side effects were remarkably infrequent. The usual side effect of gastrointestinal irritation observed in the use of erythromycin, chloramphenicol, and the tetracyclines was difficult to evaluate in patients having diarrhea and vomiting as part of the disease process. In patients with no antecedent gastrointestinal difficulty, gastrointestinal irritation was not marked. Novobiocin was administered to 20 patients with one toxic reaction. The reaction, urticaria and a diffuse morbilliform rash, promptly subsided when the drug was discontinued. There were no penicillin or known streptomycin reactions in this group of patients. Bacitracin was used very cautiously, although nephrotoxicity is reported to be less in children than in adults.[7] Blood urea nitrogen values were obtained prior to, and twice weekly during the course of treatment. Urinalyses were performed prior to treatment, on alternate days during bacitracin therapy, and several days after therapy. In only one of the 27 patients treated with bacitracin was the blood urea nitrogen significantly elevated. In this patient it returned to normal after discontinuation of the drug. A second course of bacitracin was subsequently given to the same individual with no ill effects. Microscopic examination of the urine revealed cylinduria rather consistently on the sixth to ninth days of bacitracin administration. This was a transient phenomenon and casts disappeared from the urine without reduction of the drug dosage. Proteinuria was present in many of the seriously ill patients, but was not sufficiently increased by administration of bacitracin to warrant discontinuation of the drug. None of the patients treated with bacitracin had any clinically obvious residual renal damage. Renal function tests were not performed. Three patients receiving bacitracin had marked eosinophilia ranging from 21 to 45 per cent. This, too, was reversible when the drug was discontinued. Thirty-six patients treated with kanamycin were subjected to a similar observation of the renal status. Blood urea nitrogen determinations were done prior to, and twice weekly during therapy and for several weeks afterward. Daily microscopic examinations of the urine were performed. In no instance was the blood urea nitrogen elevated above the level associated with the original disease. Coarse granular casts were observed in most patients receiving as much as 50 mg. per Kg. per day of kanamycin. Casts disappeared promptly when the dosage was lowered or the drug discontinued. Reports of toxicity to the eighth cranial nerve following administration of kanamycin prompted appraisals of hearing acuity in older infants and children.[8] No deficit was noted on physical examination. A 12 year old boy who had received 35 to 50 mg. per Kg. per day for 95 days had no gross loss of hearing. A 6 year old girl who received 15 to 50 mg. per Kg. per day had normal hearing on audiometric testing. In the newborn infants assessment of hearing was not possible.

The causes for failure of therapy in the 33 patients who died are listed in table 7.

TABLE 7

CAUSES FOR FAILURE OF THERAPY IN 33 DEATHS DUE TO STAPHYLOCOCCAL DISEASE

Late institution of therapy.
Poor host response.
Improper selection of antimicrobial agent.
Localization of infection in site inaccessible to drainage.
Irreversible tissue damage.
Superimposed infection.

Discussion

The influence of the condition of the host (age and degree of maturity) upon the course of staphylococcal disease is clearly evident from the data presented here (Table 3). Morbidity, mortality and relapse rate were all higher in the newborn age group than in older infants and children. The inability of the newborn child to localize staphylococcal infection is shown by the percentage of newborn babies with disseminated disease as compared to the percentage of older infants and children with multiple sites of involvement (Table 3).

The initial site of infection and the duration of infection prior to treatment had a direct relationship to outcome. The mortality rate was seen to be highest in patients with septicemia regardless of the age of the patients (Table 2). Because of the ability of the staphylococcus to destroy tissue the duration of the infection, of course, influenced response to therapy. In several instances where treatment was begun late in the course of the disease the infection was brought under control but tissue damage was irreversible.

In the description of the treatment of the 204 children in this study erythromycin, chloramphenicol, novobiocin and the tetracyclines have been referred as "bacteriostatic" and penicillin, streptomycin, kanamycin, and bacitracin as "bactericidal." They are classified as to their principal mode of action upon staphylococci in accordance with the data of Wise and Yow.[5,9] The importance of the bactericidal activity of an antibiotic is not established, however, it seems logical that this mode of action may be more effective than a bacteriostatic effect in the treatment of the newborn with an immature defense mechanism. In our series of cases kanamycin and bacitracin were highly effective against the staphylococcus both *in vitro* and *in vivo*. As in the use of any drug, the potential toxicity of these drugs must be weighed against the seriousness of the patient's illness. Until the side effects of these two drugs are better understood they should be reserved for use in patients with serious infections.

Emergence of strains of staphylococci resistant to kanamycin and bacitracin was not a problem in the individual patient while under treatment. Thus far, no naturally occurring "kanamycin resistant" strains have been isolated, so it is possible that this drug may continue to be useful in the management of infections caused by the staphylococcus which so readily adapts itself to many of the presently available antibiotics. However, if emergence of resistance to kanamycin and bacitracin does occur, it will probably be at a slower rate than has been experienced in the use of the more widely administered antibiotics since the potential toxicity of these drugs should limit their indiscriminate use.

Adequate surgical drainage of lesions is essential regardless of the choice of antimicrobial agent because of the ability of the staphylococcus to remain viable within abscesses. In instances where it is difficult to accomplish adequate drainage it may be advisable to instill a bactericidal solution directly into the infected cavity.[10]

Summary and Conclusions

1. Analysis of the antibiotic management of 204 cases of staphylococcal disease in infants and children is presented. Sixty-six of these patients had mild disease and 138 had moderately severe or severe involvement. Eighty per cent of the infections were hospital-acquired and 20% were nonhospital-acquired.

2. The age of the patient influenced morbidity and mortality. In the 138 patients with serious staphylococcal disease the mortality rate was 43% in the premature infants, 26% in the full term newborn infants, 21% in children from 2 months to 2 years of age, and 12% in older children. The degree of dissemination was related to the age of the patient, demonstrating inadequacy of host defenses in the young infant.

3. The selection of the specific antibiotic agent for the treatment of staphylococcal disease depends upon the age and condition of the host. In older children, or patients with normal defense mechanisms, mild and moderately severe staphylococcal infections can be expected to respond to treatment with bacteriostatic antistaphylococcal drugs. Controlled studies are needed to establish the best method of management of mild, superficial infections in the newborn. Even moderately severe infections in the young infant must be considered potentially dangerous because of the in-

fant's inability to localize infection and should be treated with a bactericidal antistaphylococcal drug. The prognosis of severe staphylococcal disease in all age groups is so grave that intensive therapy with a bactericidal antibiotic or a combination of a bactericidal drug and a bacteriostatic drug is indicated.

Acknowledgments

Disk and tube dilution tests for antibiotic susceptibility of the strains of staphylococci were performed by the Jefferson Davis Hospital Laboratory, The Ben Taub Infectious Disease Laboratory, and the Houston City Health Department Laboratory, Houston, Tex. Phage-typing studies were conducted by Dr. J. V. Irons, Bureau of Laboratories, Texas State Board of Health, Austin, Tex.

Kanamycin was provided by the Bristol Laboratories, Syracuse, N. Y., and Multidisks were supplied by Consolidated Laboratories, Inc., Chicago Heights, Ill. This study was supported in part by Bristol Laboratories, Syracuse, N. Y., and Pfizer Laboratories, Brooklyn, N. Y.

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Discussion (Abstract)

Dr. N. Joel Ehrenkranz, Miami, Fla. Dr. Yow and her colleagues are to be congratulated for a fine presentation of critical and careful work. In particular, I should like to draw attention to their high standards of clinical and bacteriologic diagnosis in separating staphylococcal infection from other diseases associated with a staphylococcal carrier state. There is at times a tendency to confuse these and this may lead to erroneous conclusions.

The marked superiority of bactericidal therapy in this group of infants and children is particularly noteworthy. Since it is not clearly understood how either bacteriostatic or bactericidal drugs work, we cannot intelligently discuss their different mechanisms. Nonetheless, a few speculations do not seem out of order. The bactericidal drugs for staphylococci,—penicillin, streptomycin, kanamycin, bacitracin, vancomycin and ristocetin, may need less participation by the host to overcome infection than bacteriostatic drugs. They may penetrate an infected site better, either intracellularly or into an abscess, loci where the host's immune mechanisms have difficulty operating. In sublethal concentrations bactericidal drugs may increase enzymatic susceptibility or osmotic fragility of the bacteria to the extent that rupture of leukocytes in abscess sites provides a *coup-de-grâce* for the organism. Evidence exists for increased osmotic fragility of kanamycin-treated bacteria. It is not unreasonable to assume that inability of the infant to localize infection is associated with an inability to sequester and shield bacteria from antibiotics. Thus, the penetration and the effect of bactericidal agents may be enhanced under these conditions in the newborn.

Whatever the mechanism, any infection with an over-all mortality of 43% in premature infants and 26% in full-term infants deserves prompt administration of our most potent medicines. Early treatment with bactericidal antibiotics for staphylococcal infections in infants for a duration of 5 to 10 days by a parenteral route, followed by bacteriostatic agents, orally, might lower mortality and lessen morbidity with a minimum of injections. Since resistance to the newer bactericidal drugs appears to develop slowly, combined therapy is not necessary and repeated courses are possible.

Dr. G. E. Thurman, New Orleans, La. Dr. Yow has detailed beautifully the current problems concerned with management of staphylococcal infections—with emphasis on those acquired in our hospitals. There is little that can be added, but I would of course like to emphasize and reiterate:

We are convinced that the most important mode of transmission of staphylococcal infections in young patients is "by hand." While dust and fomites also have admittedly great importance, the single factor we usually find to be most obvious is a break in requirement for frequent and adequate handwashing—whether with detergents or soaps.

We have great difficulty in appreciating the gravity of infection in some infants. We are familiar with examples of fatal sepsis with postmortem evidences of extensive necrosis in various structures, in which the infants had apparently no symptoms to cause alarm until the last few minutes or hours of life. Also, we know that blood cultures in the neonate commonly yield organisms which are ordinary respectable pathogens and which are associated with no evidence of disease whatsoever at any time. I mention these dilemmas only to emphasize the inadequacies or confusions of clinical criteria by which so many infections in infants and small children can be appreciated.

Because it is generally true of hospital cross-infections that for each one recognized clinically there are several others incubating or silent, I think we should give serious thought to modifying the usual pattern of *transferring* patients who develop any clinical evidences of infection to another part of the hospital; this "barn door" practice more often than not complicates the epidemiologic pattern and makes, through new potential foci, the problem of control much more difficult. Preferable, it seems to me, is maintaining the

position of the patient while further improving our isolation and care technics.

There is often a temptation for advising mass prophylaxis, and this temptation we ordinarily resist except in a few very special explosive closed outbreaks; examples are well known and need not be reviewed here. There are, however, several criteria by which prophylaxis for individual infants may be justified—such as premature rupture of the membranes, an obviously septic mother, precipitate and contaminated or prolonged instrumental delivery, problems in resuscitation of the infant requiring extensive manipulation through the upper respiratory tract, and perhaps, finally, "knowledgeable intuition." Actually, I suppose all these criteria might be considered together under the last heading! Ideally, when prophylaxis is to be given, it should be directed against the organism known to be causing the infections we are trying to prevent; thus there can be no "standard" drug or regimen that would be satisfactory in all such situations.

Dr. Yow has adequately emphasized the importance of using bactericidal rather than bacteriostatic drugs in most of the situations in which she has been concerned; this is nicely attested by the fatality rates she has shown to be roughly twice or more greater for comparable infections receiving bacteriostatic drugs as for those receiving bactericidal agents. For this same reason, obviously, it is necessary that our laboratories "keep ahead," if we are to succeed further in our continuing battle to keep ahead of "new" resistant organisms.

Finally, a very practical point should be emphasized that patients with apparent infections admitted to our hospitals should be rigidly isolated, that all patients should be discharged as promptly as possible to limit the opportunities for exposure (even under the best conditions), and that reasonable follow-up studies should be made for all hospitalized patients to be sure that they do not develop their nosocomial infections soon after return to their homes.

The Proctologist Must Teach*

MARK M. MARKS, M.D., *Kansas City, Mo.*

A CHAIRMAN'S ADDRESS can usually be listed as being "for good and welfare." The title of this one, "The Proctologist Must Teach," is intended for that purpose but also expresses a hope, and perhaps indicates a way for a brighter future for the specialty of proctology. Why must the proctologist teach, and who will accept his instruction? These questions can be readily answered. We have recognized the fact that the proctologist must be more than an astute diagnostician,—a skillful surgeon. In teaching he can find the limits of his knowledge, and by teaching he can extend his knowledge still further. In this field of medicine, as in others, the physician's stature grows not only because of an ability to restore health and well-being, but also for a willingness to share the benefits of his acquired wisdom and thinking with others.

An important part of this learning through teaching is in his everyday contact with fellow physicians. Opportunities of this kind are many and can be echoed in the experiences of everyone. Here are random examples: (1) A psychiatrist found that a long disturbed patient who complained of rectal discomfort had more than one illness. Under general anesthesia it was disclosed that a large fibrotic anal ulcer had eroded into the musculature. Two weeks following its surgical correction, the patient was discharged from the psychiatric section and returned to normal life. (2) A frantic bride, whose marriage was about to be annulled because of intractable dyspareunia, was referred by her gynecologist who could find no cause for it and thought perchance there was a proctologic reason. The removal of a long-standing ulcer on the anterior anal surface, along with several adjacent infected crypts and hypertrophied papillae, solved the problem and saved the happiness of two people.

In a discussion with another gynecologist the conversation turned to the treatment of acute bartholinitis. It was suggested that this entity could well be treated in the same manner that so many proctologists have learned to treat pilonidal disease. This idea was passed to others and now the operation is listed on the surgical schedule as a marsupialization or an eventration procedure. What was once a problem of first incision for drainage with a second operation later for removal of the gland, with a long and painful convalescence, is now resolved to a simple correction with a rapid and painless recovery.

A consultation with a dermatologist to discuss a puzzling case led to a joint study of the relationship between hydradenitis, perianal pyoderm and acne conglobata. When a urologist asked what anatomic structures were involved in doing a transrectal prostatic biopsy, it was not difficult to draw the parts in sagittal section for illustration. He then requested assistance in obtaining a prostatic specimen by this route. The practicability and usefulness of the operation became evident to both after it was done. Stimulated by this experience more procedures of this type were carried out jointly by other proctologists and urologists who found new values in sharing responsibility in a problem of mutual interest.

It has been more than a half century since the founding fathers of our specialty began their struggle for better care of people. Yet the number of patients that come to us who have had previous operations with unhappy results has not decreased. In many schools and hospitals proctology, particularly the anorectal portion, continues to be the stepchild in the art of healing. This still occurs because the training of medical students, interns and residents in the basic fundamentals of diagnosis and treatment of anorectal disease is often left to those who are not well informed, nor sufficiently interested to impress their students with the necessity of learning it. One generation passes this negative attitude toward proctologic diseases to the next and the trail of disillusioned patients continues to grow.

*Chairman's Address, read before the Section on Proctology, Southern Medical Association, Fifty-Second Annual Meeting, New Orleans, La., November 3-6, 1958.

How often do we see a traumatized anus caused by a well-meaning doctor in his futile attempt to force a thrombosed anal vein into the rectum in the honest belief that he was reducing a prolapsed hemorrhoid? What of the constant misuse of antibiotics and suppositories in the misguided presumption that these would cure thrombosed hemorrhoids, fistulas or abscesses? How many physicians make no effort to examine the anal outlet as part of the physical examination, and if they did would they recognize an abnormality? Does their inexperience or reticence in doing a proctoscopy cause them to miss the detection of early malignancy? What of the physicians who still believe that only after the childbearing period is a rectal operation on a woman of permanent value? Why is there a continued paradoxial feud between proctologist and general surgeon? Questions of this kind are many. They point to erroneous concepts which have their origin in a gross defect in medical education.

I do not speak of those schools of medicine where qualified proctologists give adequate instruction in the diagnosis and treatment of proctologic disease. Unfortunately, there remain teaching institutions which pride themselves on the excellence of their training, and justly so, yet offer their undergraduate and graduate students little or no instruction in our specialty. The proctologist has a vital stake in these matters, for only by his continued efforts to bring an awareness of this neglect will there be a realization that this, too, is a dangerous stumbling block in medical progress.

In those hospitals where the proctologist has recognition, he can maintain contact with students as well as graduates and stimulate interest by demonstration and discussion. He can and should assist in setting standards of professional competence for other staff members and offer himself for whatever instruction is required. Residents in medicine should be as well versed in the use of proctologic examining instruments as they are in handling the ophthalmoscope or stethescope. Surgical residents should know how to cope with proctologic emergencies and possess a good working knowledge of the anatomy and physiology of the parts in relationship to adjacent structures. The proctologist has much to gain in being the guiding hand in this instruction, for it is through his constructive efforts that better medicine in this specialty will be practiced.

He also has a duty as a teacher to his patients. An important part of any treatment is to inform the patient and to explain the nature of his ailment whenever that is feasible. A simple explanation, the showing of a photograph or a drawing will frequently alleviate unnecessary apprehension and enable the physician to obtain more satisfactory cooperation through better understanding.

We learn from each other because experience first instructs the individual who increases this acquisition by contact with his colleagues. The exchange of ideas propagates still more thinking and enriches the fund of knowledge that finds fruition in the satisfaction of better care for our patients. It has been truthfully said that nothing is so well done but that a better way is possible. The constant modification of standard procedures attests to the fact that progress in any field of endeavor is a restless, relentless force that cannot be denied. Our work is no different in this regard. Because of it, meetings such as this must be held, new instruments and technics devised, papers written, and the truth pursued by whatever means we can contrive. For these and many other reasons the proctologist must continue to teach.

Shotgun Wounds of the Hand and Wrist: With a Report of Four Cases*

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A functioning hand is the most essential attribute of the extremities. Thus the management of the mangling effects of a shotgun blast is of the highest order of importance.

SHOTGUN WOUNDS of the hand and wrist are a special type of acute injury. These multiple low-velocity missiles, especially at close range, are highly destructive, crushing, and penetrating; they usually injure muscle, tendon, nerve, and bone, as well as skin, and leave an open, untidy wound. Add to this the danger of tetanus infection from horsehair wadding that is often shot into the wound, and one has a formidable situation that challenges even the best surgical skill.

Treatment

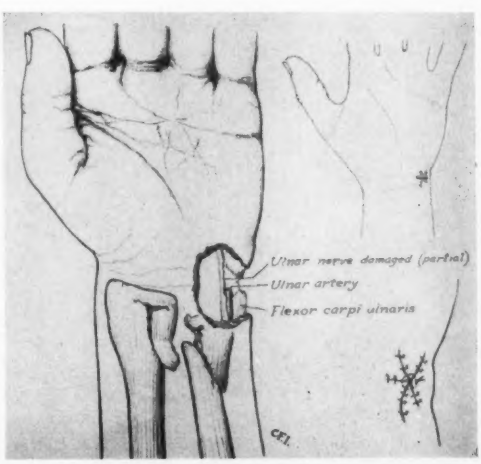
If definitive treatment is not immediately available, only the following primary procedures should be carried out: control of the major hemorrhage, usually by covering the wound with a pressure dressing and elevating the extremity; splinting of the hand to prevent painful movement during transportation; injection of a suitable antibiotic; and sedation of the patient.

Time is of the essence in preventing infection. The surgeon and the operating room must therefore be made available to the patient without delay, regardless of previous commitments. The surgeon must also have the patience to do the job adequately as well as immediately, for his initial care is far more important than the remainder combined.

On arrival the patient should be examined for shock. Blood transfusions should be ordered if needed, preoperative medication given, and the patient made ready for a general anesthetic after routine laboratory tests of blood and urine and after examination of the heart and lungs. To minimize contamination, the wound should be examined only once before operation, and then by the surgeon who will do the operation. Care should be taken not to breathe or talk into the wound. Also at this time an estimate should be made of any vascular impairment to the fingers and hand, so the patient or his family may be informed before operation whether amputation is being considered. Skin loss should be determined so that preparation may be made for grafting if necessary. If one suspects the need of a large split graft from the thigh, or an abdominal flap graft, a general anesthetic is mandatory. Otherwise a brachial block may be used if the surgeon prefers.

Nerve damage also can often be diagnosed at initial examination. The surgeon may note any loss of sensation over the areas innervated

FIG. 1

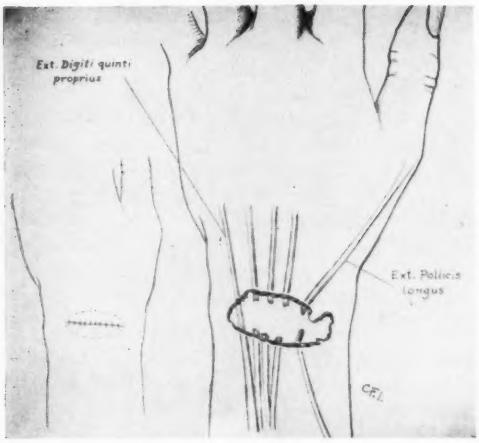


(Case 1) Preoperative analysis, volar view.

*Read before the Section on Orthopedic and Traumatic Surgery, Southern Medical Association, Fifty-First Annual Meeting, Miami Beach, Fla., November 11-14, 1957.

†From the Campbell Clinic, and the University of Tennessee College of Medicine, Memphis, Tenn.

FIG. 2

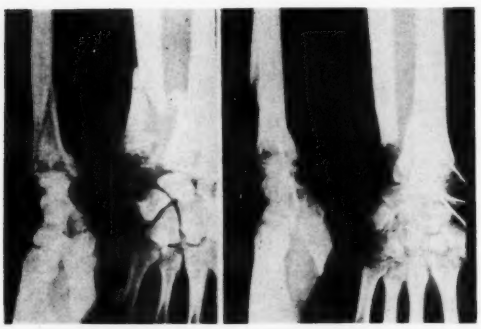


(Case 1) Preoperative analysis, dorsal view.

by the radial, median, and ulnar nerves. If the patient is able to perform thumb opposition, the motor branch of the median nerve is intact. The function of the deep motor branch of the ulnar nerve can be determined by having the patient abduct the index finger, either by pinching against the thumb or against the examiner's resistance. This causes the first dorsal interosseus to contract, the last muscle innervated by the ulnar nerve.

Tendon injury can often be suspected by the relative position of the fingers. The finger with both deep flexor tendons severed usually rests in an extended position compared to the adjoining undamaged digits. If the examiner gently manipulates the finger tips, the involved finger offers less resistance.

FIG. 3



(Case 1) (A) Preoperative roentgenograms. (B) Roentgenograms immediately postoperative.

Often the wound is so painful that the patient cannot cooperate by repeatedly moving his fingers, but with encouragement he may try once to grasp with his entire hand, thus giving a clue to the careful observer.

X-ray examination should be made to determine bone damage and the resting-place of any lead pellets.

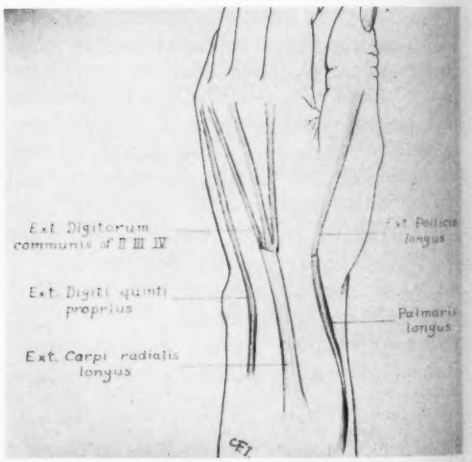
These preliminaries should take place within fifteen to twenty minutes. Operation is then performed under tourniquet control and general anesthesia (or a brachial block if preferred).

The surgeon must remember three cardinal principles in treating the severely injured hand. Though they have often been expressed in other words, I call them the three cardinal C's: *Clean—Cover—Correctly position.*

Cleaning is begun outside the protected wound with soap and water and should extend above the elbow. The hair should be shaved and the skin scrubbed with a brush or rough cloth. The wound itself should then be irrigated with a steady stream of water; it should not be subjected to a brush or to rough gauze but gently massaged with the gloved hand. The amount of water used should be measured in gallons, not in quarts. After the wound is thoroughly irrigated, the skin only is prepared with an antiseptic.

A discriminating and orderly *debridement* follows, along with further irrigation. Embed-

FIG. 4

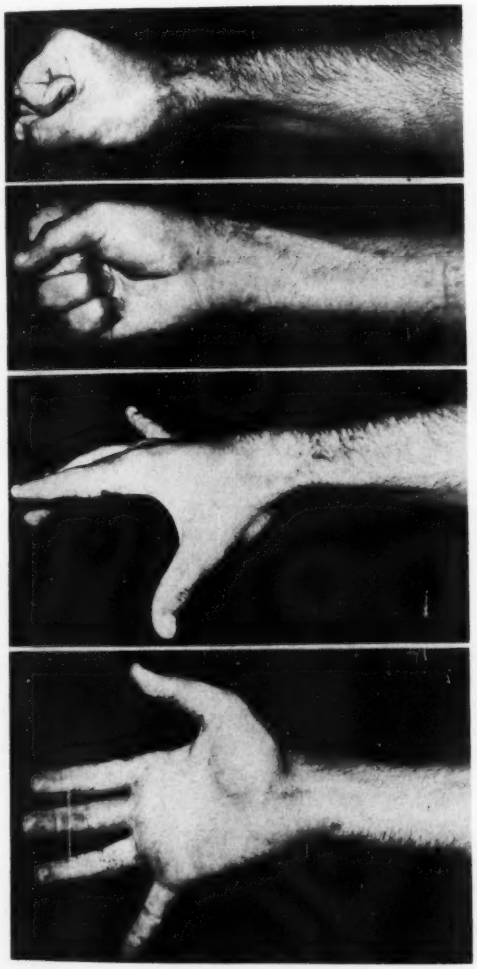


(Case 1) Tendon transfers for restoration of function.

ded lead pellets are removed if encountered, or if lodged in a joint space, but otherwise are left alone. Special care should be taken to seek for possible embedded horsehair shell wadding. If the blast was at close range, wadding is nearly always present unless it has passed completely through the wound. In cutting away devitalized tissue, one should not remove nerve tissue, regardless of how severely contaminated it may appear. All major tendons are saved and plans are made to cover them adequately. Tendons of secondary importance, such as the palmaris longus, the proprius extensors of the little or index fingers, and possibly the wrist flexors or sublimis tendons may be sacrificed, if indicated, with less functional loss than with the loss of profundus flexors and long finger and wrist extensors. Bone fragments should be saved if attached to soft tissue, and removed only if lying free in the wound. Of course the distal end of the ulna may be removed if necessary with little functional loss. Skin should be removed only if devitalized.

Except for skin coverage, little if any repair should be attempted at this time. Kirschner wires may be used to restore the bony archi-

FIG. 5

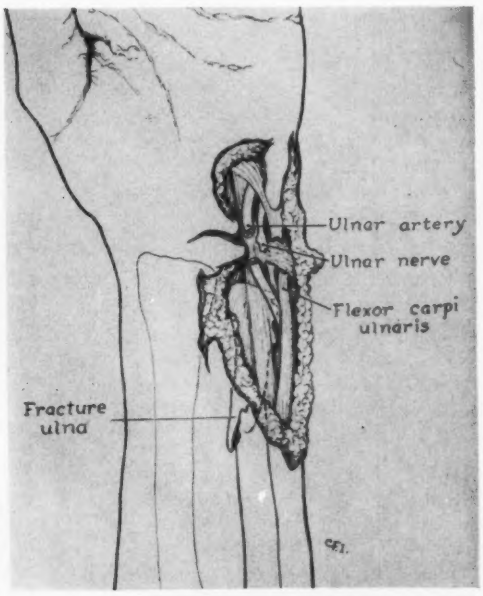


(Case 1) Postoperative functional result.

FIG. 6

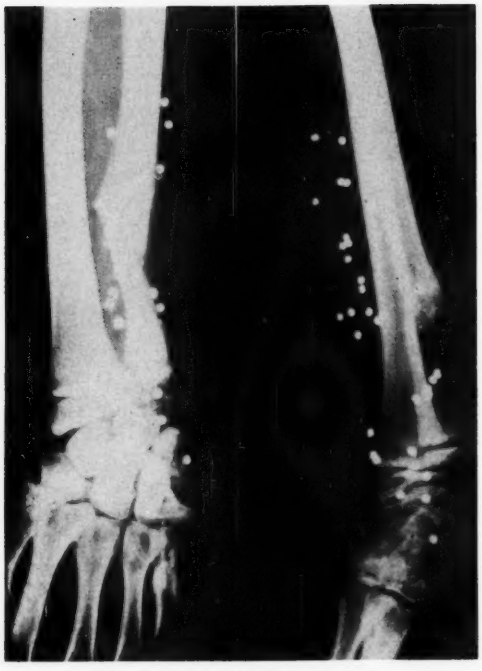
(Case 2) Preoperative photograph.

FIG. 7



(Case 2) Preoperative analysis.

FIG. 8



(Case 2) Preoperative roentgenograms.

tecture. These small wires are a great asset in the transfixation of metacarpal bones, or in medullary fixation of phalanges; a frame may thus be preserved on which to assemble the remaining soft parts at a later date.

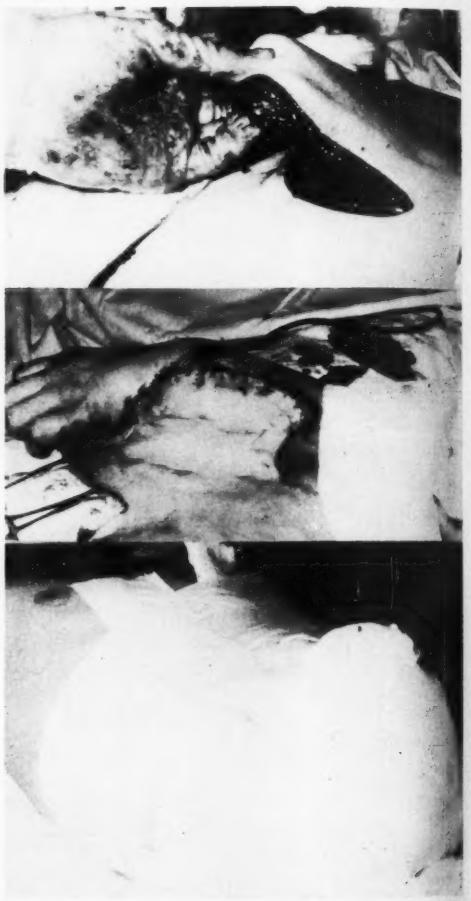
Tendons should be sutured only in rare circumstances, and then with fine multiple-filament wire using the simplest stitch, such as the double right-angle suture. Nerves should be sutured only if they can be covered by well-vascularized tissue, for example by placing them between layers of muscle.

Before the second C, *Cover,* is considered, the tourniquet is released and the hand held with a pressure dressing for 10 minutes. The vessels are clamped and tied with suture no larger than 000 catgut. Prevention of hematoma is essential.

To *cover* the exposed raw surfaces, at least a split-thickness skin graft must be used. Small split skin grafts the size of postage stamps can be obtained from the forearm with a razor. But exposed tendons, nerves, and bones require both skin and subcutaneous tissue coverage to survive. At times, a local skin flap may be developed to cover these vital structures. On the dorsum of the hand, sliding the surrounding tissue over the wound after an elliptical excision is often possible (Fig. 2), creating a transverse suture line. If the defect is large over the exposed bones, vessels, and nerves, an abdominal flap may be necessary, for if these are not covered, function of the entire hand may be lost.

The immediate covering of the wounded hand with skin is a necessity peculiar to the hand. Wounds in other parts of the body, such as the calf, thigh, or upper arm, do not require this immediate coverage and may, in fact, do better with delayed coverage. In the hand, scar production and tension lines must

FIG. 9



(Case 2) Immediate application of an abdominal skin flap to cover exposed bones, tendons, and nerves.

FIG. 10

(Case 2) The abdominal flap 5 weeks postoperatively.

be minimized by immediate replacement of lost skin.

Drainage should always be established from the wound, as further hemorrhage or infection may otherwise prove disastrous.

Correct positioning is the third cardinal C. With the hand in the position of function, a voluminous, evenly-placed pressure dressing is applied. The finger-tips are left uncovered to act as indicators for any circulatory deficiency. In spite of repeated emphasis on "the position of function," it is easily ignored by the surgeon who attempts to treat a single component, say a fracture, by placing the hand in what he considers a more desirable position. The more damaged the hand, the more important it is to maintain the functional position.

A roll of cotton sheet wadding is wrapped over the pressure dressing, and over this a slab of plaster is held with a two inch circular roll bandage. This enables easy inspection of the wound and reapplication of the plaster shell. It also permits swelling to take place without the dangers attending an enclosed cast.

The hand is elevated immediately after dressing, and kept elevated postoperatively. Tetanus antitoxin and antibiotics are given postoperatively. The patient is kept on strict bedrest and watched carefully for infection. The hand is dressed and the drains removed as indicated, usually on about the fifth postoperative day. At the end of 4 to 6 weeks, reconstructive surgery can be begun, if no gross infection has occurred in the meantime.

FIG. 11

(Case 2) Closure of the abdominal defect.

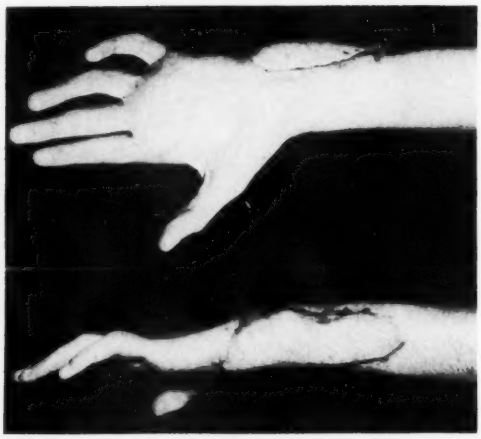
Case Reports

Case 1. A 19 year old boy was asleep in a duck

FIG. 12

(Case 2) Roentgenograms taken 3 months after initial injury.

FIG. 13



(Case 2) Degree of extension of fingers, revealing the effect of ulnar nerve palsy still present 6 months after suture.

blind when he was awakened by the yell of his companions, "Here they come!" At this he leaped to his feet with both hands raised over his head just as a hunter shot a 12-gauge blast at the flying ducks. The charge entered the ulnar and volar aspect of his right wrist at the level of the pisiform bone and came out the back of the wrist (Figs. 1 and 2).

Analysis. The wound of entry at the distal ulna at the volar crease was about one inch in diameter; the wound of exit over the dorsum of the wrist was 1 by 3 inches, but the loss of skin was not severe enough to warrant plans for skin grafting, since dorsiflexing the wrist would relax the skin and enable the defect to be closed with local tissue. The flexor carpi ulnaris tendon was severed; so were the ulnar artery and the extensor tendons of the thumb, index, middle, and ring fingers. The motor part of the ulnar nerve was partially severed. Compound comminuted fractures of the radius and ulna were demonstrated by x-ray (Fig. 3, A).

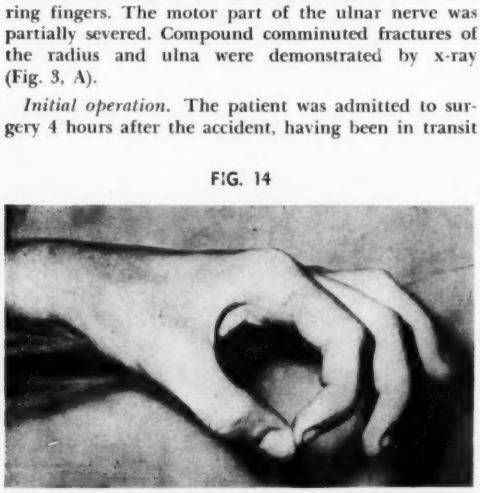
Initial operation. The patient was admitted to surgery 4 hours after the accident, having been in transit most of this time. The hand was thoroughly cleansed and irrigated. The unattached bony fragments were removed and the distal ulna resected because of severe comminution. The distal radial fragments were held in place with oblique Kirschner wires (Fig. 3, B). The exposed ulnar nerve was carefully inspected for an exact appraisal of the damage. The devitalized ends of the long finger extensor tendons were cut off, but the tendons were not sutured. The devitalized skin edges of the larger dorsal wound were excised in the shape of an ellipse so that they could be sutured to form a transverse suture line (Fig. 2). Number 35 monofilament wire suture was used. Dorsiflexing the wrist helped to relieve tension on the skin.

The wound of entry at the volar side of the wrist was closed by bringing the finger-like projections of skin together with an apical stitch (Fig. 1). A soft rubber drain was left in this wound and removed 4 days later. A pressure dressing was applied and the hand held in the position of function by a slab of plaster.

While waiting for the radius to heal, finger motion was made possible, in spite of the loss of finger extensors, by using wire and rubber bands as a substitute for the severed tendons. The fingers thus remained supple.

Reconstruction. This was begun 3 months later. The palmaris longus tendon was transferred to the long extensor of the thumb, and the extensor carpi radialis longus was transferred to the extensors of the index, middle, and ring fingers (Fig. 4). Permission

FIG. 14

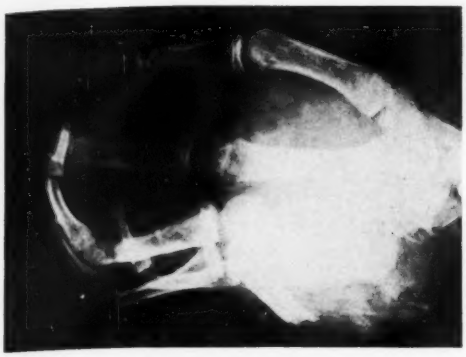


(Case 2) Nine months after suture of the ulnar nerve; power of the first dorsal interosseus muscle has returned to enable satisfactory pinch.

FIG. 15

(Case 3) Preoperative photographs.

FIG. 16



(Case 3) Preoperative roentgenogram.

was not obtained to suture the damaged motor portion of the ulnar nerve, but fortunately most of its function later returned.

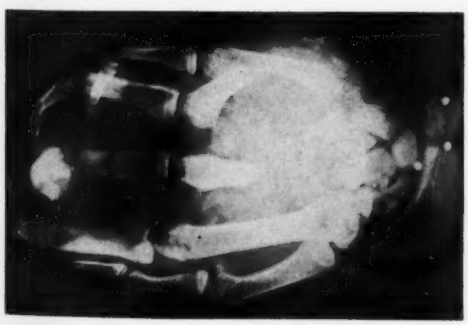
Result. Four months later, the patient's ability to open and close his hand is shown in figure 5. He still lacked normal sensation over the little finger. Pinch was impaired by the weakness of the first dorsal interosseus; nevertheless, the general function and use of the hand was satisfactory.

Comment. Note that detailed repair was not attempted initially in this contaminated and severely injured hand. The hand was cleaned and then covered. The bones were either excised or held with Kirschner wires, and the hand placed in the correct position so that tendons could later be sutured or transferred as described.

Case 2. A 12 year old boy picked up his 12-gauge gun by the end of the barrel and accidentally shot himself through the ulnar aspect of the left forearm and wrist. He was admitted to surgery 4 hours after the accident, the delay being due to transportation.

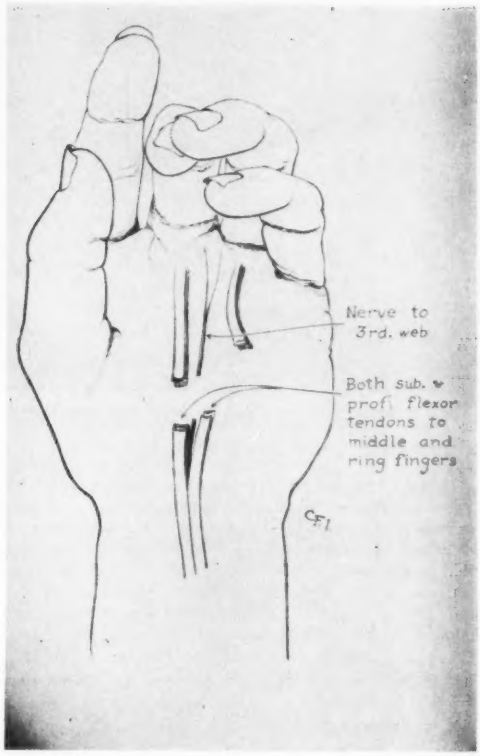
Analysis. On initial examination, a large soft-tissue defect was evident, 3 by 5 inches (Fig. 6). The flexor carpi ulnaris tendon, the ulnar artery, and the ulnar nerve were destroyed over a 2 inch area (Fig. 7). There were compound fractures of the ulna, pisiform, hamate, and fifth metacarpal bones (Fig. 8). It was evident that to save the function of the hand a skin flap would be needed immediately to cover the exposed bones and tendons.

FIG. 17



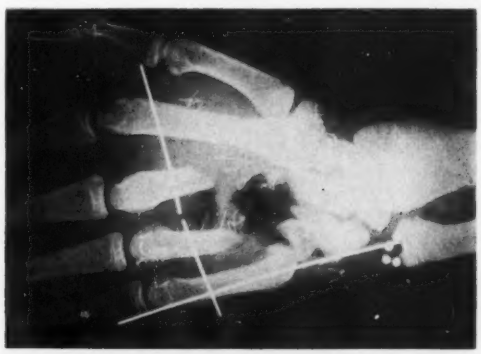
(Case 3) Preoperative roentgenogram.

FIG. 18



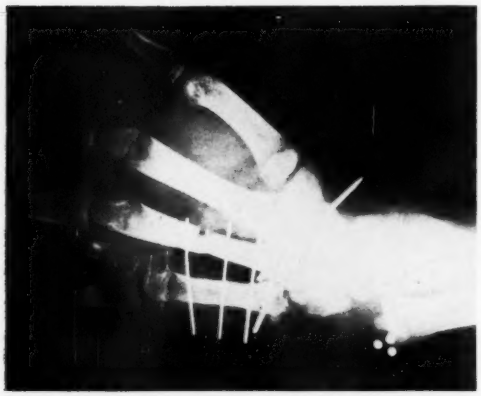
(Case 3) Preoperative analysis.

FIG. 19



(Case 3) Immediately postoperative roentgenogram showing bony fixation with Kirschner wires.

FIG. 20



(Case 3) Roentgenogram 5 weeks after initial injury showing transposition of little finger and bone graft to third metacarpal.

Initial operation. A transfusion of 1,000 cc. of blood was administered during the procedure. The wound was cleaned and irrigated thoroughly by one surgical team while another developed an abdominal skin flap that was to cover the debrided wound (Fig. 9). A split-thickness skin graft covered the exposed areas of the skin flap and abdomen. No repair was attempted of bone, tendon, or nerve. Postoperative infection fortunately did not develop, and the flap graft covering the previously exposed bone, tendon, and nerve survived (Fig. 10). It was detached from the abdomen 5 weeks later and the abdominal defect closed (Fig. 11).

Reconstruction. Three months later the ulna had healed in acceptable alignment in spite of its neglect (Fig. 12). There was no indication for repair of the flexor carpi ulnaris tendon. The ulnar nerve was sutured 3½ months after the initial injury; sufficient length was gained to overcome the defect by transferring it around the elbow and flexing the wrist.

Result. Six months after suture of the nerve, the boy had protective sensation at the end of the little finger and some return of motor power in the first dorsal interosseus muscle. The degree of extension in his hand can be seen in figure 13. He had full flexion. Nine months after initial suture, he demonstrated excellent power in the first dorsal interosseus muscle (Fig. 14).

FIG. 21

(Case 3) Completion of coverage of dorsum of hand.

FIG. 22

(Case 3) Completion of bony union.

Comment. This case is an example of a wound that must be covered with a skin flap in order to save the exposed tendons, nerves, and bone. This is, of course, an heroic approach and admittedly a gamble, but it offers the only chance to salvage the function of the hand.

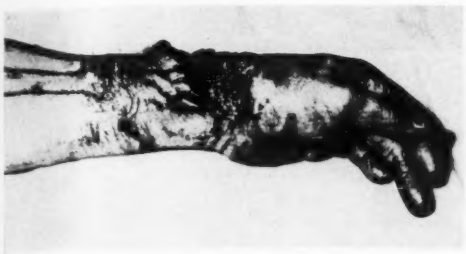
Case 3. A 14 year old boy was cleaning a 12-gauge gun; it discharged a blast that entered the midpalm of his hand and came out the dorsum (Fig. 15).

Analysis. The patient had a soft-tissue defect in the

FIG. 23

(Case 3) Photographs demonstrating finger function.

FIG. 24



(Case 4) Preoperative photograph.

palm 1 inch in diameter, and one over the dorsum 3 inches in diameter. There were compound fractures of the shafts of the third and fourth metacarpal bones, the hamate, and the capitate (Figs. 16 and 17). Both flexor tendons of the ring finger were severed, and the extensor tendons of the middle, ring, and little fingers were severed. The third common volar digital branch of the median nerve was also interrupted (Fig. 18).

Initial operation. The patient was operated on 6 hours after the accident. It was necessary to give 1,500 cc. of blood. The hand was cleaned and debrided. The distal segments of the third and fourth metacarpals were cross-pinned with Kirschner wires to maintain length (Fig. 19). The large dorsal defect could not be closed by local tissue because of loss of skin, and was unfortunately left open. It was packed with gauze. The patient had no fever after one week.

Reconstruction. At 5 weeks a skin flap was placed over the dorsal defect. The bony defect at the base of the third metacarpal was replaced by a bone graft held with Kirschner wires (Fig. 20). The fourth ray was removed and the little finger transferred to close the gap. It was felt expedient to amputate this ray because none of its flexor or extensor tendons were intact and one digital nerve was severed. The pedicle flap was completed 17 days later, covering the entire dorsum of the hand (Fig. 21). Subsequent healing of the bones is shown in figure 22.

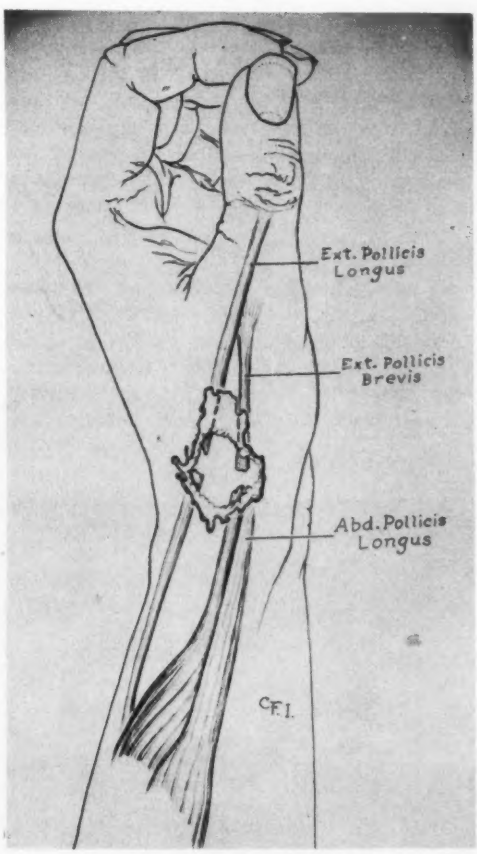
Result. After discharge from the hospital, the patient was followed in the outpatient department and was last seen 7 months after the accident. At that time he had full range of motion in his thumb and full flexion of the middle and distal joints of the index and middle fingers, but only a few degrees in their proximal joints. Extension of the middle joints was limited to 50 per cent. The little finger was markedly limited in motion (Fig. 23).

Comment. This patient might possibly have had a much better functioning hand had a skin flap been applied initially, but this procedure was considered too dangerous at the time, for the wound went completely through the midpalm and left much devitalized tissue. A temporary split-thickness graft

FIG. 25

(Case 4) Preoperative roentgenograms.

FIG. 26



(Case 4) Preoperative analysis.

might have been used to cover the large palmar defect.

Case 4. A 30 year old man who dropped his gun while attempting to shoot a chicken received a 12-gauge shotgun blast in the radial aspect of his wrist (Figs. 24 and 25).

Analysis. The patient had a tangential wound at the radial styloid with a soft-tissue defect of ½ by 1½ inches. The abductor pollicis longus and extensor pollicis longus and brevis tendons were severed. The distal radius and navicular were comminuted. Small sensory branches of the radial nerve were cut (Fig. 26).

Operation. The patient was operated on about 2 hours after the accident. The wound was cleaned and the abductor pollicis longus tendon sutured with multiple-filament wire to its distal end and to the distal segment of the extensor pollicis brevis. This repair was considered reasonably safe because the wound was not large and could be covered by surrounding skin. Removal of the detached bone fragment at the radial styloid (Fig. 27) enabled easier skin closure with #35 wire. A pressure dressing and cast were applied.

Result. The wound healed with a minimum of drainage within 3 weeks. The tendons remained intact. The thumb remained stable and lacked only the last 20° of complete extension at the metacarpophalangeal joint (Fig. 28).

Comment. The bones, tendons, and soft tissue could in this case be given definitive treatment primarily, because the wound was small and could be adequately covered by adjacent skin.

Summary

Shotgun wounds of the hand and wrist are highly destructive of the compact structures of muscle, bone, nerve, and tendon as well as skin. Immediate proper care is needed to prevent deformity, malfunction, and further damage from infection. This initial care is summed up in three principles, the *three cardinal C's:* Clean, Cover, and Correctly position. Definitive surgical repair must usually be postponed. Meanwhile the wound should be thoroughly irrigated, carefully debrided, covered either by local skin or an appropriate skin graft, and dressed with the hand in the position of function, a position which should never be sacrificed in favor of treating just one component of the multiple injury. Four cases illustrate these principles, and suggest how far one may venture toward complete repair at the initial operation. Usually, repair of nerves and tendons must be postponed from 4 to 6 weeks; meanwhile, Kirschner wires may be useful in maintaining the bony architecture until reconstructive surgery is safe.

FIG. 27

(Case 4) Immediately postoperative roentgenogram.

FIG. 28

(Case 4) Functional result.

Discussion (Abstract)

Dr. Seymour Morse, Jacksonville, Fla. Dr. Milford has collected four interesting cases of shotgun injuries of the hand and wrist. In studying his objectives and results, I feel that certain points should also be emphasized as well as those described. The utilization of his easily remembered format as the three cardinal C's should assist the surgeon in recognizing the requirements to obtain the best possible hand for function.

Cleaning of the wound offers several interesting points for discussion. There are those who feel that copious irrigation of the wound is detrimental and that thorough debridement is the method of choice.

In the latter technic, due recognition is given to the importance of leaving uninjured nerves, vessels, tendons, joint capsule, and all available skin.

Removal of foreign bodies is important, as those near a joint or near the grasping portion of the hand. Metallic fragments seldom cause delayed healing but it is the nonopaque objects, as clothing, dirt, and gun wadding that may be the source of further trouble.

I should like to hear more emphasis on the treatment of fractures initially. They should be set and placed in good alignment early. This may be done with mild traction or even pin-fixation. Correction of alignment restores muscle balance and this permits the hand and wrist to assume positions of function. Following skeletal correction and splinting in the position of function, efforts may be devoted toward keeping the hand mobile.

I agree with Dr. Milford's emphasis on the second C,—cover for tendon, bone, or joint. Primary coverage should be considered initially and should be accomplished without tension on the wound edges, for sutures are likely to pull out with resulting scar. If unable to close the wound simply, then closure at angles may be considered with use of a skin graft. When the skin graft is considered, the full thickness abdominal pedicle graft is preferred to the split thickness graft.

A fourth C may be added, i.e., commencement of early motion. All uninjured parts should begin motion early and continue persistently. Injured parts should be splinted in the position of function during convalescence, but motion should be encouraged soon thereafter. Unusually stiff joints should be aided by the use of splints and elastic springs.

I would like to compliment Dr. Milford on his cases and their discussion. Its timing is seasonal. Most important in surgery of the hand is the surgeon. If I may be permitted to quote the late Dr. Bunnell, "Hand surgery is an area specialty, not a tissue specialty. . . . Most men earn their living by their hands. How much it must mean to the patient to restore to him what he has lost, when that loss is the use of his hands."

HOTEL RESERVATION APPLICATION FORM

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Some Considerations Concerning Chicken Bones in the Esophagus*

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The author discusses the reasons for an increasing incidence of chicken bones as a foreign body in the esophagus. Diagnosis and treatment present certain problems of which the surgeon must be aware.

ONE OF THE EARLIEST RECORDED REFERENCES to removal of a bone lodged in the esophagus, according to Jackson,[1] is found in Aesop's fable of the Wolf and the Crane about 500 B.C. This fable tells of a wolf that gulped his prey so rapidly and with such poor mastication that a bone lodged in his throat. Whereupon, he ran through the land howling and offering a reward to anyone who would remove it. A crane moved by pity and desire for reward undertook the dangerous task. Having successfully removed the bone the crane asked for his reward. To this the wolf replied, "What could you possibly require? You have put your head in my mouth and instead of biting it off I have let you pull it out unharmed. Get away with you and don't come again within reach of my paw." From this Dr. Jackson assumed that human nature had not changed greatly in the past 2,500 years.

Chicken bones lodged in the esophagus have become of increasing interest to the medical profession in the past 10 to 15 years due, in part, to the very rapid growth of the chicken industry. This is more especially emphasized in the southern states where broiler production has blossomed into a major source of farm income in many states.

The State of Georgia may be used as an example to show the rapid increase in chicken production in the South.

FIGURES FOR GEORGIA AND UNITED STATES

1935	
Ga.—500,000 broilers	$ 231,000.00
U. S.—Chickens	$ 232,000,000.00
1956	
Ga.—222,780,000 broilers	$ 129,836,000.00
U. S.—Chickens	$1,028,000,000.00
1957	
In the 10 Southeastern States—	773,809,000 broilers
1958	
Ga.—Broilers in excess of	300,000,000
1940—U.S.	
Per capita consumption of broilers	14.1 lbs.
1957—U.S.	
Per capita consumption of broilers	25.3 lbs.

Review of the Literature

One of the most beautifully tabulated and indexed works on foreign bodies in the air and food passages was presented to the American Laryngological, Rhinological and Otological Society by Chevalier Jackson in 1923.[2] He not only described 1,155 cases, but did so with pictures of the foreign bodies and descriptions of the methods used for removal. In very few of these cases was anesthesia of any type used, and it is remarkable to consider the difficulties thus imposed on the operator. In that series of cases he listed 8 chicken bones, 7 of which were of a flat variety and one of which was spicular. Six were located in the esophagus, usually in the coronal plane. One was in the larynx and one in the trachea. Compared to that series it is of considerable import to note that of 250 cases of foreign bodies in the air and food passages reported from the Chevalier Jackson Bronchoscopic Clinic in 1943, by Norris,[3] there were 28 chicken bones. This rather dramatically points out the relation between the increase in consumption of chickens and the presence of chicken bones in the esophagus. Improvement in diagnostic procedures over that 20 year interval may also be partly responsible. Another finding reported in the latter series was that 74% of the bones found in the esophagus were in patients over 40 years of age. It is probable that the presence of den-

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tures is one of the chief factors in this, since the patient with an upper denture generally does not feel the bone until it has passed the palate. This is often brought out in the history. Jackson[4] reported, in 1936, that dental plates were, on occasion, responsible for ingestion of foreign bodies. The most emphatic discussion of this relationship was Reading's[5] report, in 1939, stating that of 40 patients who swallowed bones in his series 39 had upper dentures. (He reasoned that American dentists were more conservative than English dentists and so more dentures were present in his series from England.)

Feder and Meyers,[6] in reporting on swallowed foreign bodies, pointed out that in 71 instances of swallowed foreign bodies 51 passed the esophagus and all but 3 of these passed through the gastrointestinal tract successfully. One of the 3 was a chicken bone which, interestingly enough, lodged in the rectum. Matheson[7] included 151 meat bones in his series of 602 cases of esophageal foreign bodies, and emphasized that the most common location in the esophagus was at the cricopharyngeal sphincter.

When bones lodge in the food or air passages, over 90% occur in the esophagus according to Jackson.[8] Of 2,461 foreign bodies in the food and air passages, 387 (15.7%) were bone, and 355 (91.7%) of these bones were in the esophagus. The average stay of the foreign bodies in the esophagus was 3.9 days in the series of Hung and Lin.[9]

Jackson[10] has stressed the use of x-ray films as a help in diagnosing foreign bodies of the esophagus, but warned that calcifications of the tracheal and laryngeal cartilages may be mistaken for foreign bodies.[4] This point was recently re-emphasized by Richardson[11] who reported a case of calcification of the cricoid cartilage masquerading as a foreign body in the esophagus. Norris[3] pointed out that nearly all chicken bones in his series were sufficiently radiopague to be seen in the lateral neck film, but in a few instances a barium swallow was necessary to confirm the diagnosis. This brings up a point which seems to need emphasis. The lateral neck film will usually show incarcerated chicken bones in the esophagus. The postero-anterior view rarely shows them to any degree, yet often these cases are seen after having been told there is no foreign body simply on the basis of a film in this view. If only one film is taken, it must be a *lateral* one, to take advantage of the odds, since the portion of the chicken most often encountered is a flat bone which, if viewed on edge, casts a definable radiopaque shadow. In my experience, if the lateral view of the neck fails to show a foreign body and considerable doubt still exists as to its presence, it may be preferable to proceed with an esophagoscopy. This is better than to depend on a barium swallow since so much spasm may exist that much of the barium may be retained in the area of the foreign body and make its identification and removal more difficult. However, this is personal preference and I do not mean to be tedious over a point in technic which is equivocal.

Many complications may follow the ingestion of bones, including peri-esophagitis and/or abscess and mediastinitis with or without perforation of the esophagus. Cases have been reported of bones perforating the esophagus and presenting in the cervical area or in the trachea. One of the most dreaded complications is perforation of the aorta by an esophageal foreign body. Barrie,[12] in 1946, stated that between 1840 and 1940 there had appeared 74 published cases of such a tragic accident; one was definitely due to a chicken bone (15 were unspecified bones). In such a case reported by Haines,[13] due to a chicken bone, there was no x-ray evidence of the bone prior to death.

Diagnosis and Treatment

Often the history is in itself practically sufficient to make the diagnosis. Bearing in mind that esophageal foreign bodies of a bony nature are more often found in the age group over 40 years, probably because of upper dentures, and that the cricoid area is most often affected, a tentative diagnosis is often established. An x-ray film is then in order remembering that with flat bones the postero-anterior view may be negative, and that a lateral view is necessary. Care must be exercised not to confuse calcification of laryngeal cartilages with bony foreign bodies. If the x-ray film is not diagnostic, one may choose between proceeding with esophagoscopy or using a barium swallow, depending on which has been more successful in the physician's experience.

In doing an esophagoscopy for removal of a chicken bone considerable care is necessary to prevent overriding, since the bone is usually flat, located in the coronal plane and in the cricoid area. It has been my experience that more spasm in the cricoid area is encountered under local anesthesia and, since this may actually tend to cause perforation by a sharp bone, the use of general anesthesia with an intratracheal tube is utilized unless contraindicated by the patient's general condition. The relaxation thus afforded reduces the effort necessary in removing the bone and so lessens chances of perforation. The bone should be carefully examined before being grasped, and if a sharp point can be disengaged it should be. Recently an article appeared which suggested transecting the foreign body with scissors before removal; this certainly may be indicated if any undue resistance is met in attempting removal. Here my experiences suggest that rotation forceps are preferable to firm grasping forceps, since rotation forceps allow the bone to turn gradually to the diameter best suited to its removal and tearing of tissue is less likely.

FIG. 1

FIG. 2

The following case histories will serve to emphasize some of the more important points in diagnosis and treatment.

Case 1. V. L. S., a 37 year old negress, 5 days prior to admission was eating chicken dressing when she felt something catch in her throat. This was associated with considerable pain and discomfort on swallowing. During the following 4 days she was able to take only small amounts of liquids. When seen in the office she localized her pain over the cricoid area.

The larynx and hypopharynx were clear. T. was 99°, B.P. 130/70, P. 72, and R. 16. The general physical examination was negative. She wore an upper denture. The WBC was 6,700, with 63% polymorphonuclears. The Hgb. was 12.8 Gm. X-ray films showed what the radiologist defined as a spicule of bone measuring 26 mm. in length by 1 to 1.5 mm. in width lying 1 cm. below the inferior level of the thyroid cartilage (Fig. 1).

Accordingly, an esophagoscopy was done, and a large flat, thin bone, apparently from the breast bone of a chicken, was found in the indicated area and was removed without difficulty. The postoperative course was uneventful.

Case 2. L. M. T., a 57 year old white woman, was eating creamed chicken on the day of admission when she felt something stick in her throat. She was taken

to the hospital where x-ray films were made. A foreign body was defined lying anterior to C6-C7, and appeared 3 cm. long and spicular, according to the radiological diagnosis (Fig. 2). The patient located her discomfort to the cricoid area.

The larynx and hypopharynx were negative, as was the general physical examination. The patient wore an upper denture. The WBC was 7,650 with 67% polymorphonuclears. The Hgb. was 11.7 Gm.

An esophagoscopy was done and a large, flat piece of chicken breast bone was removed from the described site without event. The postoperative course was uneventful.

Case 3. C. J., a 68 year old white woman, was seen approximately 3 hours after having eaten some chicken and having the sensation of something lodged in her throat. She located the difficulty at the level of the cricoid.

The general physical examination was negative. She wore an upper denture. The Hgb. was 10.6 Gm. The larynx and hypopharynx were clear. An x-ray film showed a calcified shadow at C6-C7 which seemed linear and measured 20 mm. by 3 mm. (Fig. 3).

At esophagoscopy a flat, wedged shaped piece of breast bone of chicken was removed from just below the cricoid area. The postoperative course was uneventful.

FIG. 3

Case 4. A. L. C., a 52 year old white woman, was seen 4 days after eating chicken and having the sensation of something lodged in her throat. Swallowing became progressively more difficult during the intervening time until only ice could be taken.

The general physical examination was essentially negative. She wore an upper denture. X-ray films showed a foreign body at the level of C5-C6 with compression of the overlying trachea. The T. was 101°. The WBC was 9,100 with 66% polymorphonuclears. The Hgb. was 12.5 Gm.

At esophagoscopy a foreign body was located just below the cricoid. Considerable inflammatory reaction was present. Because of the flat shape and the sharp edges of foreign body, removal was tedious and difficult, but finally a large, flat piece of chicken breast bone was removed. The postoperative course was satisfactory. The temperature gradually returned to normal and the patient made a complete recovery.

Discussion

These 4 cases tend to emphasize certain facts which stand out as important in the diagnosis and treatment of chicken bones in the esophagus. First, all of the patients wore an upper denture. Second, in all cases, although a competent radiologist took and read the films, the patients were thought to have spicular pieces of foreign bodies present until esophagoscopy actually proved them to be flat pieces of bone, which apparently are much more common for chicken bones than are the spicular ones. Third, and this is a personal observation, I have not been able to clearly verify in any other series, women seem to be effected more often than men. This conceivably might be due to a slightly smaller size of the esophagus in the female, or even to the shape of the larynx in the female. One other thought is that women conceivably may more often eat the type of chicken, such as creamed chicken or chicken dressing, which is more likely to contain a flat piece of chicken bone. At any rate, in my experience women have been more commonly effected. Fourth, it is emphasized, indirectly, that younger people are not so prone to have retained bones as foreign bodies, as they occur more commonly in patients over 40 years of age. Finally, all of these foreign bodies were located in or near the cricoid area and in the coronal plane, which is the most common place for these flat bones to become lodged.

It seemed obvious, in reviewing the literature concerning chicken bones in the esophagus, that prophylaxis might hinge on two main factors. First, the presence of the bone

in the food, and second, the presence of an upper denture. After long discussion with several prominent dental surgeons, it has been impressed upon me that it is highly unlikely, in the immediate future, that any upper denture can be produced which will help the situation. The upper denture is partly held in place by suction and fenestrating the upper plate would greatly reduce its efficiency. Also, if a soft material were used in the center frequent replacement would be necessary and fit would be erratic. Consequently, efforts toward prophylaxis seem to center around removal of the bone from the food. This can be done at the home level, but how much better it would be if the chicken processing centers could undertake the job. Because of the frequency with which the breast bone is involved, if this particular bone could be eliminated many of our worries concerning chicken bones in the esophagus could be over. If we, as physicians, strongly urge the removal of the breast bone of the chicken at the processing plants I believe it would not be long before this could become an established procedure. Already many plants offer the breast meat as fillets with the bone removed; an extension of this method would seem the best logical prophylactic measure.

Summary

1. The literature concerning chicken bones in the esophagus has been reviewed.

2. Cases emphasizing points of diagnosis and treatment have been presented.

3. Increasing numbers of chicken bones in the esophagus may be anticipated as chicken consumption increases.

4. Prophylaxis may best be achieved at present by removal of the bone from the chicken, preferably at the processing plants.

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Discussion (Abstract)

Dr. Harry Zoller, New Orleans, La. I really enjoyed this paper and the manner in which it was presented. I recently had 3 successive cases in which the patient swallowed a chicken bone, with x-ray evidence of the foreign body, and on esophagoscopy no chicken bone was found. These patients were again examined by x-ray and the same foreign body shadows were present.

A study of the literature later convinced me that after 20 years of age ossifications may occur in the thyroid, cricoid, arytenoid, tertiary cartilages and lateral hyothyroid ligaments, and that these shadows often are confused with the presence of a foreign body. Since over 90% of the foreign bodies of the esophagus are below the cricopharyngeus muscle, one is almost certain of the presence of a foreign body if a shadow is present below the lower border of the cricoid cartilage, as seen on a lateral roentgenogram of the neck.

Whenever in doubt, it is better to do an esophagoscopy than allow the foreign body to perforate, since one then has a more complicated situation.

On Psychic Factors Conditioning Effects of Drugs in Psychiatry*

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That there are psychiatric factors in the apparent effects attributed to drugs *per se* have been shown in a convincing manner.

IN PSYCHIATRY drugs are being used in variety and quantity to produce behavioral and emotional changes in the patient. Little is known concerning the role of the personality and the social field in determining the appearance and the nature of effects of drugs. The data in this paper are gathered from the authors' experience as participants in a psychiatric unit where drugs have been used for both treatment and research, and from a review of the significant literature.[1-4] These data suggest a series of hypotheses applicable to research and clinical usefulness of drugs currently in use in psychiatry (i.e., phenothiazine compounds and derivatives of Rauwolfia).

We wish to review briefly the model of drug action in general medicine for purposes of contrasting it with a suggested model of drug action in psychiatry. The classic model of the use of a drug in general medicine may be summarized as follows: a drug is given which has specific physiologic effects such that either a remission is produced directly as with, for example, digitalis; or where a remission is allowed or facilitated as with, for example, the various antibiotics. These changes are on the physiologic level, and all occur within the circumscribed universe of the individual patient's physiologic state. The physician has an active role in the cure, but as a nonparticipant, at least in respect to the processes of change in the patient's disturbed physiologic processes. The physician assists and supports the disturbed physiologic state of the patient, through medications and by supporting the patient psychologically. But the physician does not become a part of that disturbance, nor does he become a part of the specific processes involved in physiologic healing.

A model of drug action in psychiatry is reminiscent of this, but there are differences. In psychiatry a drug produces various specific physiologic effects. In general these effects are unknown. Where we do know some of the physiologic effects, we do not know their significance for later changes in feeling and behavior. Somehow, as a result of the physiologic effects of the drug, there appear behavioral changes in the social field. It is this —the change in the patient as a member of various interpersonal relationships—which is sought through the effects of the drug. Thus the area where "healing" processes take place, is not within the circumscribed universe of the patient's disturbed physiologic state, but within the extended area of the patient's interpersonal living (past and present). In a sense, we give drugs to affect the group, considering the patient as a member of a group.

In psychiatry, effects of drugs are thus a consequence of:

1. The specific physiologic effects of the drugs.

2. The personality structure of the patient.

3. The structure of the milieu within which the drug acts on the patient. There are some reasons, derived from clinical observation, to suggest that the last two factors are the most significant, once a drug has some sort of general effect, and that of the last two—the structure of the milieu—is of considerable significance.

Heretofore much of the attention paid to the psychologic part of "psychopharmacologic

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technics" has been in terms of either the placebo effect, or the effects of suggestion, including compliance of the patient and other similar phenomena under the heading of suggestion. These two operations occupy only a small part of the psychologic area in drug action.

We may hypothesize that the specific physiologic effects of the drugs produce changes which are limited and conditioned by the personality structure of the patient, and limited, conditioned and directed by the social milieu of which the patient is a part. Though most of the specific physiologic effects of the drugs are unknown, and connecting links between these effects and emotional and behavioral changes are unknown, the personality structure of the patient, and social structure of the milieu may be studied in some detail.

The ego structure of the patient determines partly what the effects of the drug may be.[2] For instance, in giving chlorpromazine to certain schizophrenic persons, it has been observed that when there occurs decreased motility and decrease in sensory inflow associated with the administration of chlorpromazine, some patients respond with increasing anxiety. This increasing anxiety may be followed by deeper regressions and by episodes of hyperactivity. In other schizophrenic patients given mepazine, which is sometimes associated with a euphoric-like effect, patients have responded with paranoid delusions that some substance was being given which was stirring up their sexual needs. Other patients have responded with considerable anxiety to physiologic effects of the drugs, claiming that they were being embalmed, etc. It is of course well known that certain patients respond to drugs derived from Rauwolfia with increasing depression.

In considering the effects of the social field upon drug effects, the ego structure of the patient is of course important,—for example the need for dependency. A patient who is heavily tranquilized may become threatened by the increased dependency facilitated by the decreased motility. Consequent anxiety may be enhanced or decreased by environmental response to this dependency. Whether or not the patient is generally compliant or rebellious within the social group will have a determinant effect. The extent to which the patient is unconsciously sensitive to, and willing to meet the unconscious needs of the staff who are giving the drug, and the staff's expectation of drug action, is of considerable importance.

In general, the effects of the milieu on drug response may be classed under three headings. These are:

1. What the milieu expects.
2. What the milieu will allow.
3. What the milieu will deny or reject.

The term milieu is considered to include the total interpersonal relationships in the ward group, the administrative hierarchy, and the unconscious wishes, needs and expectations of the patient in question, the staff, and other patients. The effects of the wishes of other patients is a significant and often a factor which is overlooked. It is sometimes striking to see a patient respond quite convincingly in a "tranquilized" manner when he has been given some nonsedating drug. When this is explored it appears that other patients have told the patient what to expect and have encouraged him to develop the seemingly appropriate response.

The expectations of the milieu exercise a conditioning effect on drug effects. On some wards one sees a much greater tranquilizing effect of chlorpromazine than on others. On some wards there is seen a higher incidence of minor side-effects than on others. On some wards specific beneficial effects of drugs appear much more often than on others. We have observed that with a drug (mepazine) which does not produce somnolence or decreased motility, many nurses on certain wards, and even patients report increasing somnolence and decreasing motility with great enthusiasm, in the context of the patient "improving."[1]

The limits set by the ward group are significant. For instance, on some wards somnolence is frowned on as perhaps a complication, and even something which is a little disgraceful in the patient. On wards where considerable aggression is allowed, we see patients showing increasing activity even with various drugs producing decreased motility. On wards where interpersonal relationships are facilitated, we may see the nurses proudly reporting that since a patient has been taking

large doses of chlorpromazine he has been much more active socially!

These areas of behavior or change which the milieu will either deny or reject are especially important in conditioning drug effects, and are important in generating what we term "interpersonal complications" of the drugs. Interpersonal complications are considered to be specific complications arising from the administration of a drug, but appearing on the interpersonal level rather than the physiologic. They are thus analogous, but not equivalent, to physiologic complications of the use of drugs in physical disease. On certain wards we have observed instances in which patients become markedly worse with the administration of drugs. We have observed two major sequences under these circumstances. The first is where the patient gets better and makes sexual advances toward the nurses. These may be rebuffed, even though the sexual overtones were little more than a technic for seeking contact, and the patient experiences increasing isolation and anxiety. A few days later this has progressed to excitement or increasing delusional formation, and it is reported that somehow the drug has made the patient worse. Another sequence is seen when, associated with administration of a drug, the patient becomes somewhat more aggressive, complaining or demanding. Here again feelings are aroused in the staff which have as a consequence the patient's being isolated or rebuffed. Again a few days later, it is reported that the drug "worsened" the patient's condition. A contrariwise complication, perhaps more frequent though more difficult to see in operation, is the following sequence. A patient brought into the ward disturbs staff and other patients alike with a variety of technics. A drug is administered which has as one effect somnolence and a slowing-down. Other patients and staff report cheerily that the patient is so much better, and unconsciously encourage the patient to maintain a more-or-less fetal state.

There are a number of clinical and research applications for these hypotheses and observations. In administering these drugs the clinician is faced with the questions of what changes will the milieu permit. This is of concern within the hospital and the family. In considering the individual patient a number of questions are important. How will the patient's concept of his body image be affected by the drug? How will the patient react to a decrease of motility? Will the patient be threatened, for example, by the appearance of increased dependency needs?

The research implications of these observations and hypotheses are evident. In studies of drug effects where the locus of change due to the drug is in the interpersonal area, a thorough knowledge of the structure of the milieu, as well as the changes allowable and sought for within that milieu on both a conscious and unconscious level, is necessary as controls in research. In this type of research the observer must thus be a participant observer. A further implication is that research into the phenomena of social and psychic conditioning of the appearance and type of drug effects is a field of study in itself.

In the preceding sections we have not been discussing whether or not drugs are beneficial or harmful in some cases; we have not been discussing whether or not we choose, by preference, to use or avoid these drugs. We have been considering some of our observations and hypotheses on the mode of action of these drugs, and some of the factors which condition this mode of action.

We have found that it is quite difficult for the physician to observe and study the sequences outlined in this report for a number of reasons. First of all, when these drugs are used, the physician is a participant in the relationships and social structure which determine to a significant degree what the effects of drugs will be. Another factor which accounts for this problem is that the mode of action departs from the classic medical model of drug action. The extended field of drug action, and the extended field of process impinging upon the drug effects in the patient precludes the classic model of drug action. A further point is that these notions are useful regardless of whether the person administering the drugs uses concepts of emotional, physical or mixed etiology of the phenomena associated with the psychiatric illness.

Summary. Examination of differences between the classic model in medicine for drug action, and the model useful for study of drug

action in psychiatry reveals that in psychiatry there is an extended field of process which affect and condition drug effects. Data have been presented to illustrate this hypothesis. The data suggest that the social field—the milieu—exercises a significant effect on the appearance and type of drug effects in psychiatric illnesses.

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Topical Steroids in Diseases of the Colon*

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The use of steroids in the form of a rectal instillation may offer a valuable adjunct in the treatment of acute exacerbations of ulcerative colitis.

THE ANTI-INFLAMMATORY AND ANALGESIC ACTIONS of the corticosteroids have been well documented.[1-4] Such actions are noted when hydrocortisone or its analogues are applied to the skin or the mucous membrane of the eye, nose, or the synovial membranes of joint cavities. Topical steroid therapy has been widely accepted and extensively used in inflammatory conditions of these surfaces. Yet, there has been a peculiar reluctance to explore the use of these compounds on the accessible mucous membranes of the gastrointestinal tract. This report concerns itself with our experiences and those reports in the literature on the use of topical steroid therapy in some diseases of the colon.

Factitial or Radiation Proctitis

The term factitial proctitis was introduced by Buie and Malmgren, in 1930,[5] for those changes found in the walls of the rectum following extrarectal application of radium or radium and roentgen ray in the treatment of pelvic lesions. The degree of tissue damage varies from localized erythema and telangiectasia with a friable mucosa to ulceration, stricture and rectovaginal fistula or perforation of the bowel. The interval between the termination of treatment and the development of these changes is extremely variable from 3 weeks[6] to as late as 7 years.[7] Six to seven months has been reported as an average time of onset.[8,9] Symptoms depend partially upon the degree of proctitis and the stage of its development. Bleeding and the passage of mucus are usually the first signs.[10] As the process progresses, tenesmus, urgency, and diarrhea appear with pain and pressure in the rectum. Constipation and obstipation as a result of stricture or fear of defecation may occur, and colostomy may be required. The diagnosis is made by the history of exposure to radium or roentgen ray and the proctoscopic picture, particularly if telangiectasia is seen. The barium enema may show undue fixation of the involved segment without intraluminal defects. It may be impossible to exclude extension from the carcinoma, and often time is required to settle this issue. The process is considered to be self-limiting provided the malignancy does not recur. The interval required for healing is rarely less than 14 months and generally not under 2 years. Previous therapeutic efforts have often been unsatisfactory.

Hurtig, a gynecologist, first suggested the rectal instillation of hydrocortisone acetate in a 100 or 125 mg. dosage suspended in water or normal saline (1 to 3 oz.) once a day in factitial proctitis. In 4 patients, after two or three treatments, he noted "immediate symptomatic relief which lasted for surprisingly long intervals. Follow-up proctoscopy showed very little change, even in asymptomatic patients, except that bleeding, mucus and friability seemed decreased. Ulceration, when present, persisted but looked cleaner."[11]

Experiences reported by Sherman[9] and later by Kaplan[6,10] confirm the symptomatic improvement. These authors reported a group of patients whose course was followed at regular intervals for a period of a year after radiation treatment of carcinoma of the cervix. (Nineteen of 102 patients developed proctitis, as shown by proctoscopy, without *any* symptoms.) Treatment consisted of rectal instillations of 2.5% hydrocortisone acetate jelly (75 mg. dose per treatment)

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twice a day. In Sherman's series[9] of 28 patients with mild lesions, these had disappeared in 21 within 2 months. Among 13 patients with stricture, ulceration, and in some instances fistula or perforation, 5 healed within 3 to 4 months, 5 had delayed healing, and in 3 no change was observed. Some degree of scarring persisted in all of these patients but some of the early strictures seemd to undergo dissolution. Two patients were thought to worsen and rectovaginal fistulas occurred under treatment. No changes were noted in the rectal mucosa after 12 months follow-up in a control group of 25 patients.

Similar encouraging results with topical steroids in radiation proctitis have been reported by Schlumberger and Robert[12] of France.

We have observed 20 patients with radiation proctitis. Treatment consisted of 10 mg. hydrocortisone acetate suppositories (Wyanoid HC) or 25 mg. of hydrocortisone acetate suspended in 2 or 3 oz. of water and instilled into the rectum two or three times a day. Prompt symptomatic relief was observed in 17 of these patients, and 3 were unimproved. In 17 patients followed over six months, aside from less hyperemia and bleeding, proctoscopic healing was only observed in 4 instances.

The failure of improvement as shown by the proctoscope in our group of patients as contrasted with Sherman's[9] and Kaplan's[6,10] series, we believe is related to the differences in clinical material. Our patients represented a group referred for care because of an unusual amount of difficulty and are not comparable to a group of patients routinely followed after radiation therapy to the cervix. Another factor may be related to the much smaller dose of steroid we used. Since this is a self-limiting condition, we felt that symptomatic control was a realistic goal and was usually adequate. There is little reason to believe that topical corticosteroids could prevent perforation or fistula formation from radiation injury although their effects on the fibroblast might prevent or delay stricture.

Idiopathic Ulcerative Colitis

We have previously reported in some detail[13] our experiences and methods of treatment in 21 patients having idiopathic ulcerative colitis. Our first efforts with topical steroids were stimulated by the success noted in the symptomatic management of factitial proctitis and were limited to patients with disease involving the rectum and rectosigmoid. At the time we began this topical treatment we were not aware of similar efforts by others, but at the present time, there are at least eight similar reports in the literature from Europe and this country.[14-21] The dosage and methods of administration have varied somewhat, but all these writers remark on the rapidity of symptomatic and proctoscopic improvement.

In general, we have used three methods of therapy: (1) suppositories containing 10 (Wyanoid HC) or 15 mg. hydrocortisone acetate for mild disease limited to the rectum or rectosigmoid; (2) for further involvement of the colon, watery suspensions of 50 mg. of hydrocortisone acetate or 10 mg. of prednisone have been used in rectal instillations two or three times a day; and (3) for more extensive involvement, a daily proctoclysis with 50 or 100 mg. of water soluble sodium succinate hydrocortisone (Solu-Cortef, Upjohn) in 250 or 500 ml. of saline have been given. Treatment was usually carried out for a two week period, but if early improvement was noted upon proctoscopy and tissue changes were marked the treatment has been prolonged for several weeks. If a response is not apparent in two weeks, we believe further therapy is useless and perhaps harmful.

In our first report, we emphasized that the majority of our 21 patients had mild and early ulcerative colitis involving the rectum and rectosigmoid. For example, roentgen ray changes were noted in only 6 of the group, and only 7 had systemic symptoms. The symptoms were of recent onset in fourteen. We stressed that the over-all improvement rate of 76% was no greater than in similar reported series with this type of patient;[22,23] although the improvement figure referred to that observed with the proctoscope, the rate of symptomatic improvement was somewhat greater (86%). Bockus[22] suggests that an attack of ulcerative colitis involving the rectum and rectosigmoid is perhaps self-limiting, but by self-limiting was meant an attack lasting from 4 to 12 weeks. It was the rapidity of remission that stimulated our report, for we observed changes toward healing occurring within a

matter of days and symptomatic improvement was often noted 24 or 48 hours after treatment was started. The greatest failure rate was in the chronic group, but it was difficult to evaluate these failures. One patient with disease of the entire colon had a large rectovaginal fistula that made retention of the material impossible. Another patient with symptoms for over 20 years had multiple perirectal fistulas and abscesses, and although there was improvement in the appearance of the upper rectosigmoid, the perirectal disease continued relentlessly. This patient eventually required partial colectomy. A third patient, a 20 year old man, was considered to be a failure, although the colitis was in remission at the time treatment was started and treatment was carried out primarily for purposes of absorption studies and to note the area of colon that might be treated by proctoclysis. There were no significant changes in either the proctoscopic picture or barium enema after two weeks of treatment. The number of stools had decreased from four per day to one or two.

Since that original report, we have had the opportunity to observe 6 more patients. One of these patients with moderately severe rectal and rectosigmoidal disease and a history of recurrent episodes of colitis for five years obtained a remission as shown by the proctoscope and control of symptoms after 10 days of rectal instillations of 20 mg. Meticortelone (prednisone and prednisolone) in 100 cc. of water three times a day.

Two patients with chronic recurrent episodes of bloody diarrhea of several years duration, and with more than 50% colonic involvement as shown by barium enema developed a remission of symptoms and an improvement in the proctoscopic appearance in two and three weeks respectively. In one of these patients there was reversal of radiologic changes in a follow-up film 2 weeks later. The second patient had been on systemic ACTH at the time of admission, was febrile and was having six to eight stools per day and an equal number at night. The systemic ACTH was gradually stopped and a steroid proctoclysis of sodium succinate hydrocortisone, 100 mg. per day, was started. After 3 weeks of therapy the bowel movements had decreased to one or two semiformed stools a day and she was afebrile. A second barium enema showed no significant change. The follow-up period on this patient is 2 months, and 6 months in the other.

A fourth patient, with total colonic involvement, was admitted shortly after the fifth of a series of exacerbations she had had with ulcerative colitis in five years. Previously, she had responded to prednisone and salicylazosulfapyridine. At the time of her admission she was afebrile, but her diarrhea and abdominal cramps had recurred and the proctoscopic examination revealed a moderately granular and friable mucosa with multiple ulcerations and some few pseudopolyps. Therapy was started with daily proctoclysis of sodium succinate hydrocortisone 50 mg. in 250 ml. of saline, and after 5 days this was increased to 100 mg. in 500 ml. of saline. There was no significant change in her symptoms or in the appearance of the bowel until the second week of therapy when she noted a sudden increase in the number of stools per day and an increase in bleeding. Proctoscopic examination revealed a hyperemic and friable mucosa with what appeared to be an acute flare-up of the disease. The proctoclysis was stopped and she was started on prednisone systematically and salicylazosulfapyridine with a gradual improvement in her symptoms. The appearance of the bowel reverted to its original picture of a more chronic process one week later. She was discharged a month later after a slow but steady improvement in symptoms, but without any striking change in the proctoscopic appearance. This patient represents the only instance we have seen of worsening of the process under this form of treatment.

A fifth patient, having segmental colitis and a partial rectal stricture following a surgical procedure elsewhere, became afebrile and had cessation of diarrhea after 2 weeks of hydrocortisone proctoclysis. A month later the rectal stricture was corrected surgically and healing was not delayed. The barium enema done 2 months later showed changes toward healing. In the original films there was a suggestion of involvement of the terminal ileum. However, this is not seen in the follow-up barium enema.

One case of acute colitis was observed in a 25 year old senior medical student. He developed a respiratory infection on January 12,

1958, manifested by cough and retrosternal burning. The following day his temperature rose to 101°, the cough was loose and slightly productive. At this point, he began self-prescribed tetracycline, 250 mg. every 6 hours, and "Coricidin" tablets as needed. He remained in bed for the following two days. On January 15, late in the afternoon, he noted increased peristalsis and abdominal cramps. During the night he had 10 to 12 bowel movements which were watery, yellow and foul smelling. By the following morning there was much tenesmus, and the stools had become grossly bloody with moderate amounts of mucus. At this point he sought medical help. He appeared acutely uncomfortable and dehydrated. His temperature was 98.4°, pulse 96 per minute, and his blood pressure was 104/65. There was a slight mucopurulent exudate in the nares and diffuse abdominal tenderness with hyperactive bowel sounds. Proctoscopic examination revealed a grossly edematous and hyperemic mucous membrane which was very friable and exuded copious amounts of bloody mucus. Smears of the exudate revealed many pus and blood cells, a few gram-negative rods, but no gram-positive cocci or parasites. His hemoglobin was 17.7 Gm., the PCV. 57%, WBC 7,500, with 56 polys, 35 lymphocytes, 6 monocytes and 3 basophiles.

It had been our immediate clinical impression that this illness was an acute enterocolitis following antibiotics, perhaps due to resistant staphylococcus. When the smears did not reveal this organism, he was treated symptomatically with intravenous fluids and codeine hypodermically. His tenesmus and bloody mucoid discharge continued except for a short time after each injection of codeine, and by 10 p.m. that evening he had hardly had a moment off the bedpan and his stools consisted of bloody mucus. At 11 p.m., he was given 10 mg. of morphine; after thirty minutes 50 mg. of hydrocortisone acetate in 3 ounces of water were instilled into the rectum. The solution was retained and shortly thereafter he went to sleep. He slept soundly until 3 a.m. when he had one more bowel movement, was given another 10 mg. of morphine and did not awaken until about 10 a.m. The following day, January 17, he had one bloody mucoid movement and was given another steroid enema preceded by an injection of morphine, 10 mg. He rested quietly the remainder of the day except for a few cramps. Following this the bowels did not move for 48 hours and thereafter he had a normal formed stool daily. The steroid instillations were continued for 5 days. A follow-up proctoscopy 7 days after onset revealed a granular mucosa with some slight erythema and prominent vessels. He was discharged asymptomatic on January 24, and has had no recurrence of

TABLE 1

SUMMARY OF TREATMENT OF 27 PATIENTS WITH NONSPECIFIC ULCERATIVE COLITIS USING TOPICAL STEROID THERAPY

Classification	*Number of Patients*	*Bowel Symptoms Improved*	*Proctoscopic Appearance Improved*	*Treatment Failure*	*Duration of Remission Over Six Months*
Disease limited to rectum and rectosigmoid	20	17	17	3	14*
Acute	14	13	13	1	13
with systemic symptoms	5	4	4	1	4
without systemic symptoms	9	9	9	0	9
Chronic	6	4	4	2	3*
with systemic symptoms	1	0	0	1	0
without systemic symptoms	5	4	4	1	3*
Total colonic involvement	6	4	3	3	2
Acute	1	1	1	0	1
Chronic	5	3	2	3	1
with systemic symptoms	4	3	2	2	1
without systemic symptoms	1	1	0	1	0
Segmental involvement with systemic symptoms	1	1	X**	0	1
Total	27	22 (81%)	20 (77%)	6 (23%)	17 (62%)

*Two patients responded to a second course of therapy following a relapse 1 and 2 years later, respectively.
**Roentgen involvement proximal to rectosigmoid.
All patients, in addition, received a bland diet, antispasmodics, sedatives, blood, electrolytes, and antibiotics when indicated.

the difficulty. Stool cultures were reported as showing *Paracolobactrum aerogenoides* and *P. vulgaris*.

We do not know whether this particular illness represented an untoward reaction to antibiotics, a specific infection from an antibiotic resistant organism, or idiopathic ulcerative colitis. Nevertheless, the clinical response to topical steroid enemas was very striking and gratifying.

A retabulation of our experiences with 27 cases of idiopathic ulcerative colitis is presented arranged on the basis of anatomic involvement (Table 1).

The best results have been noted in early disease limited to the rectum and rectosigmoid. The group of more extensive colonic involvement and segmental involvement is very small and the follow-up too short to evaluate the eventual place of this form of treatment in this disease. The dramatic results we have noted in these 4 cases have encouraged us to attempt this therapy as our first therapeutic effort in these patients. All of our patients were given sedatives, blood, antispasmodics or antibiotics when they were thought to be indicated. We wish to emphasize that this method of treatment is suggested as a therapeutic *adjunct*.

The advantages of topical steroid therapy are the rapidity of response, improvement not only symptomatic but by proctoscopic examination, minimal detectable degrees of absorption[19,24-26] with avoidance of undesirable side effects of prolonged steroid therapy, and maximum concentration of the medication in the area of involvement.

The disadvantages are related to the unpredictable response, the difficulties in retention, which in most cases is related to anatomic difficulties rather than tenesmus, and, in one instance, the worsening of the proctoscopic and clinical picture under such treatment.

We feel it is imperative to follow the course of this treatment with frequent proctoscopic examinations. If a response is not obtained within the first two weeks of treatment, topical therapy should be discontinued.

Summary

Topical steroid therapy with hydrocortisone or its analogues has been used in 20 patients having factitial proctitis with prompt symptomatic improvement in 17, though healing was only observed in 4 instances.

In 27 patients with idiopathic ulcerative colitis, rapid symptomatic improvement and remissions as shown by the proctoscope were observed in 22 (81%) and 20 (77%) patients, respectively. The best results were obtained in early disease involving the rectum and rectosigmoid.

One patient who developed a severe and bloody diarrhea following oral antibiotics responded dramatically to rectal instillations of hydrocortisone.

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Discussion (Abstract)

Dr. Belton G. Griffin, Houston, Tex. It is a distinct pleasure for me to have the privilege of discussing Dr. Patterson's paper.

Every gastroenterologist is aware of the extremely variable and unpredictable course of chronic ulcerative colitis. Like peptic ulcer, we know that ulcerative colitis can, at times, for any reason or for no reason at all, go into a more or less complete remission. Most of us have had the experience of having a patient admitted to the hospital with the idea that a colectomy would probably be required, and have the patient go into a prolonged remission while we were preparing to have the colectomy done. While it is well known that many drugs may exert some influence on the course of chronic ulcerative colitis, it is also true that the sincere interest of a physician at times may seem to accomplish more than medication. No discussion of the treatment of ulcerative colitis is complete without a reference to the psychotherapeutic side of treatment. For these reasons it becomes exceedingly difficult to decide whether the good results experienced by Dr. Patterson's patients are due to the topical corticoids or to the other excellent treatment which I am sure Dr. Patterson gave these patients. Truelove's double blind control studies would seem to indicate that the topical corticoids are indeed effective.

My own experience with this method of treatment has been limited to 4 patients in whom the method was given an adequate trial and one patient who had so much difficulty in retaining the material that the therapy was promptly discontinued.

Three of the patients whom I treated are young housewives with mild to moderately severe disease. Each of them has continued to work in spite of the passage at times, of rather large amounts of blood from the rectum, and the typical proctoscopic and x-ray appearance of chronic ulcerative colitis. Each of them has learned to administer the medication at home and each has seemed to have some reduction in the amount of rectal bleeding and mucus, and each has shown considerable improvement in the proctoscopic appearance. One of these continued the therapy only a short time because she felt that it was too much trouble. The other 2 are continuing the therapy. The fourth patient whom I treated is a 45 year old man who had very severe chronic ulcerative colitis of some six months duration. The proctoscopic appearance of his bowel compares with that of the worst which Dr. Patterson demonstrated by his excellent color slides. The bowel was fiery red, almost completely denuded of mucosa, and bled freely at the slightest provocation. He was having ten to twelve or more watery, bloody stools daily. After 2 weeks on the program as described by Dr. Patterson, his bowel had an entirely different appearance. It presented a somewhat velvety appearance of an essentially normal color, certainly not like the angry, inflamed, hemorrhagic bowel seen 2 weeks previously. His clinical response paralleled the improvement in the proctoscopic appearance.

Thus, after this amount of experience with this method of treatment, my attitude has changed from one of skepticism to one of enthusiasm. If further experience demonstrates that topical corticoids can permanently protect the bowel against the ravages of this devastating disease, it is not inconceivable that major changes in our thinking on the subject of surgery for chronic ulcerative colitis may result. One might give serious thought to doing more ileosigmoidostomies and hope to control the disease in the sigmoid and rectum by the use of topical corticoids.

Again, I would like to congratulate Dr. Patterson on his excellent paper.

Public Health Aspects of the Chronically Ill and Aging*

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The socio-economic and medical problems of the aged and the chronically ill touch upon business, governmental and professional areas of our national life and economy. The impetus of this phase of our Nation's welfare is gaining a momentum which will ultimately be brought to some conclusion. It cannot reach a final, well rounded solution without the active participation of the medical profession. Organized medicine is aware of this, and this is good. But individual attitudes among the profession will determine the proper control of the solution in a given community.

FOR SEVERAL YEARS we have believed and stated that the chronically ill and aging are a public health responsibility. With each passing year this line of reasoning seems to have more basis in fact but, actually, the problem evolves about the difficulty of finding the proper persons to handle it. It would be redundant to delve into the myriad of statistics testifying that we are, paradoxically, a comparatively young nation with an ever-increasing older population. The management of the parallel sociomedical aspects of this problem has been delegated to Departments of Welfare, Public Assistance, and the like, thus placing the onus for their care in the hands of nonmedical personnel. This in our opinion creates an almost disastrous imbalance of medical and nonmedical care.

We must admit, of course, that the training of physicians in this field is sadly lacking, although in some schools here and there one finds a beginning awareness that the study of medicine embraces more than anatomy, chemistry, etc. For example, in a few schools medical students are learning about socio-economic problems in their first year along with the purely basic sciences. This is a step in the right direction, but it will require years of pressure to force medical educators to the realization that the practice of medicine, to be successful, must include at least a working knowledge of patients' problems which might influence their physical state. But tradition, although respectable, is intolerably narrow, and especially is this true of medical teaching. This same tradition places the public health physician in the category of issuing health permits for food handlers, venereal disease control, and sanitation. But we feel very deeply that public health has advanced far beyond this point and needs as well to evaluate the existing *status quo* of the chronically ill and aging. If this is not done with dispatch, a heterogeneous group of persons, unacquainted with medical exigencies, will have in their care and as their responsibility many chronically ill and aging who are not receiving adequate medical care today.

Allegheny County Program

Allegheny County (Pennsylvania), which includes Pittsburgh, and having a population of 1,700,000, now has one new county hospital, modern in every respect and with a capacity of 2,200 beds. But, if its services were available to all of the county's citizens who need to use them, at least seven or eight additional hospitals would be necessary. And, based on the cost of $22 to $24,000,000.00 for this present institution, it becomes obvious that "building more stately mansions" is not the answer for the care of the chronically ill and aging. What follows may be historical, but it does point the way to a better understanding and handling of this problem.

In 1946, after World War II, a simple program of physical restoration was inaugurated at Woodville, at that time one of two county facilities for the care of the indigent ill.

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The results attained gave evidence that not every entrant to the "County Home" would spend the remainder of his days there. The existing "gateway to oblivion" in many instances became the "revolving door," permitting not only admission to the "Home" but also return to family, community and friends. There were and still are many facets to this original problem that make for fascinating repetition.

When a catastrophic illness strikes a family the physician is naturally called. Either because of lack of help or simply for the sake of convenience, removal to a local hospital is effected; in most cases the wheel of routine then ends in the rut of indolent chronicity. Since few physicians presently practicing have received any training in the care of this type of patient, there is automatically little desire or ability to take an interest in the "old crock or chronic." It is to be fervently hoped that modern schools will strive to overcome this deficit in the curriculum. An erudite writer in children's problems once said that, "the desire for good music can be inculcated as well as the raucous ragtime or other objectionable forms of music." This principle applies as sharply in our reasoning provided that medical students and their teachers become acquainted with the groups of patients in our discussion. A simple example of the excessively blind routine so prevalent today is the diabetic who has had a stroke and who, with his family, is expertly trained in diet and the administration of insulin but receives no instruction in restorative technics. In other words, too commonly "we treat the diagnosis and ignore the disability." And too frequently we overlook the well-known fact that most problems of the chronically ill and aging are multiple and rarely consist of a single diagnosis or disability.

When the patient is discharged to his home more difficulties ensue. Since little if any direction or instruction is given at the hospital, the family often manages the patient like the first newborn. The tender loving care and over-indulgence then lead to radical and insidious changes in the patient. In this respect we classify patients in four groups as follows:

(1) Those patients who have accepted their physical misfortune and willingly, or by necessity, strive to make themselves physically and/or economically independent within the limitations set by their disabilities.

(2) Those who by pity draw to themselves excessive attention from families and friends and who, through wielding the "club of disability" become the tyrants of the household.

(3) Those who are resented by the family for having caused some disruption in the household and are consequently neglected or hidden in the back rooms.

(4) Those who, steeped in the conviction of their own limitations, resist any attempt to better their circumstances.

For any number of reasons, entry to a "county home" or "poorhouse" is the last desperate measure. The most common reason for this transfer is the removal of a wage earner from circulation to care for the patient. Adjustment from home, humble as it may be, to a public institution is extremely difficult, perhaps because of regimentation,—benign or otherwise. And too often the assigned bed is one which will most likely be occupied until death. In most county homes medical care is scanty, if given at all, except for emergencies.

Frequently a retired physician, or even one chosen on the basis of proper political affiliation, calls at the institution, dispensing "care" to his patients at irregular intervals. Registered or even practical nurses are rarely engaged, unless large hostels operate more like hospitals than "depositories."

The conditions described above are common to many of the 235 "homes" one of us (M.B.F.) has visited in the past twelve years. Except for a few physicians, a few registered nurses and "aides," the situation in Allegheny County (Pittsburgh, Pennsylvania) was about the same. But in 1946 a very simple program of physical restoration was begun. Over the past twelve years it has paid dividends not only in the number of patients discharged, but certainly in better conditions for those who must remain in the institution. A brief description of our *modus operandi* is in order. The patients are all indigent, and are admitted voluntarily after evaluation by social workers and a physician's statement. Incidentally, we are constantly amazed at the number of inaccurate diagnoses given. This, we believe, must be charged to the physician's lack of consideration for the chronically ill patient, or as a means to get him

"off his hands." Upon admission a series of moves is initiated: a complete physical evaluation, social service contact with the family, and consultations—surgical and/or otherwise—are requested by the staff physicians. This latter point is unusual in many respects. We no longer operate a surgical pavilion, referring surgical patients to our qualified consultant in this field; he in turn uses his own hospital and operating room personnel for surgery. The County pays his fee as well as the charges of the private hospital. This same procedure is followed whenever the best interests of a patient dictate removal to the hospital of any consultant. We have frequently referred to this as a "two-way street," with the private hospital and physician at one end, the public institution and staff at the other. All are dedicated to the better care of the patient which is our aim and must be recognized as such.

Eight years ago we became cognizant of the problem of incontinence, especially among our hemiplegics. We now believe, and this is factual, that "incontinence by habituation" results from too long retention of an indwelling catheter. The practice of removing the catheter, when the patient can comprehend his illness and desires, has made for easier handling of this problem in the hospitals in this area.

More recently the aging (aged) amputee has become one of our more serious problems. Although we have no complete solution it appears that we have hit on a novel but simple plan to retain more ambulation. When a human has used two legs for sixty or more years he cannot easily adjust to one leg and two crutches. We feel that the habit of continence versus incontinence as described also parallels the "twoness" of lower extremities versus the loss of one. In other words crutches are no replacement for the loss of one limb. After many attempts we believe we have solved the problem of transition to becoming an amputee. Within 7 to 10 days after amputation, and while the patient is still in bed, we apply a commercial aluminum pylon with a Thomas ring for ischial weight-bearing, a lacer and adjustable shaft. Thus, the sense of loss is less noticeable than if we were to wait out the normal time for crutches. The oldster moves the stump and pylon around and almost immediately a change to hopefulness occurs. When permitted out of bed, weight-bearing is almost immediate and the transition is complete. If the remaining leg is reasonably sound, a conventional prosthesis may be applied later. The great advantage to this procedure is that it tends to prevent the aged amputee from becoming bedfast or chairfast. After a sound trial of two years we believe that our efforts in this field have been highly successful in that patients are thereby prevented from being dumped into the category of the physically indolent chronic.

Reverting to our management of the institutional patient, our care of fractured hips has been most beneficial to the patients. Again, the patient is operated on at the consultant's hospital, returned to the "county" in 12 to 17 days, and the long road to recovery has begun.

While our department of physical medicine is not extensive, we, in conjunction with the nursing staff, train selected aides in restorative services. It would pay to give more attention to these essential persons, so necessary especially in tax-supported institutions. The required number of professionals in all fields would constitute a tremendous economic burden were it not for the classification of aides, orderlies, and attendants.

The Public Health Needs

While we have deviated to describe briefly some of our activities within an institution, the public health aspects are of far more importance, since there are more chronically ill persons outside of hospitals than within. The question of responsibility for these people is most pressing; we must blame medicine, politics, and a phlegmatic public. Organized medicine must accept the blame at all levels for inadequate care. As previously pointed out, few medical schools do anything about engendering an understanding of the social and economic lives of their "clinical material" so necessary to the student-in-training. In addition, during the clinical years very little teaching about the chronic or aging is put forth. And we are of the opinion that this is most regrettable for *every illness or injury, however minor, represents a potential chronically ill person.* This lack in his medical background inculcates an apathy on the part of the intern or resident which limits and restricts his attention to these people.

As former students and interns, the authors are well aware of this dereliction in teaching. In the lower echelon of organized medicine, few county societies can be troubled about their own county homes, nursing homes, or homes for the aged.

At the state level the same problem exists, except that state officials, elected or appointed, and the medical society usually castigate each other as befits their respective positions. We, as physicians, have always been taught that we should begin at our own lower level organization—the county. But unfortunately this has not proved to be very fruitful. Again, on the state level, rarely does the Secretary of Health, a physician, have anything to do with institutions. By some odd turn of political science, a Department of Welfare either operates or has supervision over institutions devoted to the patients under discussion. Here then emerges a nonmedical governmental agency conducting medical affairs, without either background or sound reason. Unless we physicians do something to adjust this inequity we will lose our right to leadership by default.

In the State of Pennsylvania where the same situation exists, the State Medical Society is attempting a compromise that seems likely to work and might prove to be a venture well worth emulating. A Commission on Restorative Medical Services, consisting of representatives of all disciplines of medicine, has been organized. It is hoped that the Secretary of Health will represent public health in this group. If and when the Department of Welfare has medical problems in a given institution and the local medical group does not, or cannot evaluate the deficiencies, the State Commission on Restorative Medical Services would then send a representative of the particular pertinent discipline to look at the problem. Through this means there would be sound evaluation by the State Medical Society, working as a unit and yet judging all facets of the situation. This in turn would enable the State Government to receive firsthand, realistic information and recommendations. Thus would private and public medicine work hand-in-hand with the State Government to provide proper and adequate facilities to its citizens, thereby creating the proper balance of sociomedical care for them. An additional dividend will be the help and knowledge that will accrue to the local Society which will in turn enhance its potential for good within its own locale. It is hoped that this technic will be followed elsewhere. But we must admit that there is one link in the chain which seems weak:—*training public health medical and paramedical professionals in technics directly applicable to the care of the chronically ill and aging.*

On the other hand, the term "welfare" in state or county governments carries broad implications which are seldom medical. In many instances these are "money dispensers" and not persons trained in social and medical welfare of indigent humans. Then again, in this State as well as in others, financial allotments are so low that the writers cannot see how little more than minimal care can be possible. Lawmakers try diligently to save dollars wherever possible, motivated either by a true sense of economy or as added reelection propaganda. We should not delude ourselves,—good medical care is not cheap. But persons in public life expect the medical profession to care for the chronically ill and aging, in or out of institutions, without charge or for a pittance. This, too, is unsound. Consider what might happen if our roads or other public conveniences were handled similarly!

Finally, *the public:* One segment feels that the problems of the chronically ill and aged are not their concern; another believes that government or medicine should do the worrying; the third is a vocal, reforming and often misguided group, without training or experience, which tries to plan for the aging population. But we feel that if government, medicine, and prominent educators point out the methods needed to aid these "displaced persons" the public will take up part of the slack.

While much of the preceding is in a critical vein, we must admit that there are many bright spots in the dark picture that has been painted. Home care programs, housekeeping services, and friendly visitors are being utilized more each year throughout the country. But by the same token the numbers requiring such services are increasing at an alarming rate.

Perhaps an explanation of what we are attempting to do in Pittsburgh and environs might be in order. Several years ago, the

Visiting Nurses Association (a Community Fund participant) expanded their services to include some restorative activities. Physical therapists were added, additional registered nurses and practical nurses were commandeered as well. Prescription forms were developed so that the patients leaving the hospitals for home, or those remaining at home are given excellent care. Above all, the family learns—through the Association—to lessen the burden of ignorance. The prescription is checked by the physician and his orders are carried out, even to the extent of arranging visits to the clinic or physician's office for checkup.

Patients discharged from the Allegheny County Institution District to home are visited immediately by someone from the Visiting Nurses Association so the restorative processes may be continued. The Association has engaged a physician to oversee these extended services, and to act as a liaison between the nursing and medical professions,—a rather difficult job at best. This whole system of home-institution care could be vastly improved if we were not faced with another failure in the training of physicians. Here, as well as elsewhere, talents of residents-in-training are not utilized for services to the home as part of their postgraduate work. This is a rather myopic fault in that the same medical people in training become totally dependent upon the broad services in an institution and rarely give themselves the opportunity of practicing medicine without all available hospital facilities and conveniences. If young physicians-in-training were made part of this total scheme of home and hospital care, it is our belief that not only would better care be provided but, just as importantly, the training of these people would be greatly enhanced. Finally, we are convinced that even for specialists the rigors of the general practitioner will produce a more competent specialist based on this broad experience.

This report obviously exposes a modicum of justifiable anger at the dearth of care for the chronically ill and aging. It is intended not so much as an emotional outburst, but rather as self-condemnation which might lead to self-discipline and a sense of urgency now lacking. We would therefore wish to present in generalities some of our concepts leading to better care for our less fortunate citizens.

(1) Public health physicians and their paramedical personnel at all levels should be trained to supervise both institutional and home care of the groups we are discussing.

(2) Departments of Welfare should *not* manage medical problems, but must be experienced in the capable social adjustment and administration of institutions, public or otherwise. They *must* have medical guidance and help to render a better cooperative public service.

(3) Medical schools should bend strict traditional rigidity of teaching to show students and graduates alike the many facets of a most distressing public problem.

(4) Poorhouses, almshouses and county homes must evolve from the Dickens era and strive for human rather than mere animal subsistence. This entails decent quarters, adequate medical care, and help from local public health physicians and organized medicine.

(5) Courses to acquaint physicians and their coworkers with the care of the chronically ill and aging at home and in institutions must be started as soon as feasible throughout the country. Since there are such programs in existence, it would seem practical to increase the number of persons being trained.

(6) Subsistence for the home-bound chronically ill should be adequate for their problems. We have suggested previously that with the monthly "relief check" sent to each client should be included a "suggested diet of the month" and other simple pertinent helpful hints.

(7) Proprietary nursing homes unfit for human occupancy or operated without consideration must be closed. However, operators can and must be assisted to raise their standards, slow though it may be, to accepted levels. This requires adequate funds.

(8) Decent housing must be provided. It is doubtful if private capital could or would undertake such a venture. At least a certain percentage (perhaps 5%) of all apartment housing should be devoted to the chronically ill and aged. It is important to realize that isolation of such housing leads to "legions of the damned" and for that reason the oldster

must have quarters in a more normal environment.

(9) Visiting nursing services, with all their appurtenances and allied abilities, must be put to work and expanded to areas without them. If not, we will continue to build institutions that could bankrupt any country. One cannot question the deeply ingrained human desire of the average person to live in his own home or neighborhood.

(10) Finally, let either sheltered workshops or similar ventures, by whatever name, be considered for a segment of population who want to continue active. We admit that this is a difficult and complicated enigma, but we must work toward its solution.

Summary

Public Health Aspects of the Chronically Ill and Aging? This is a problem not for the future alone; it is in our midst now, today. It deserves greater attention from medical and related fields, thus assisting those in public health to provide the sound medical care and common decency to which all individuals are entitled.

ARE YOU MOVING?

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Clinical Effects of Extreme Obesity on Cardiopulmonary Function*

V. WILLIAM COLE, M.D., and
JAMES K. ALEXANDER, M.D.,† *Houston, Tex.*

In the last several years more is being learned about the pathophysiology of obesity as related to the respiratory and cardiovascular systems. This will be shown to play a part in impairing the normal functions of the heart and lungs.

EXTREMELY OBESE PERSONS may have any of the following signs and symptoms: dyspnea, somnolence, easy fatigability, pedal edema, polycythemia, evidence of heart failure, proptotic eyes, cyanosis and Sheyne-Stokes respiration. The purpose of this report is to describe our experience with these signs and symptoms in obese persons and to present an illustrative case report.

Clinical Manifestations

In the patient who seeks medical advice because of extreme obesity, *dyspnea* is usually one of the presenting complaints. Its pattern and severity vary considerably. Nearly always dyspnea is present with exertion. The dyspnea may vary from a subjective feeling of mild difficulty in moving air to an almost total inability to breathe, and with accompanying signs of orthopnea, apprehension and sweating. The exertional dyspnea is usually rather promptly relieved by rest and sometimes by change in position. If congestive heart failure is present, it is striking to see respiratory embarrassment occur on shifting from a standing or sitting position to the supine position.

Somnolence is common in these patients. They tend to doze when unoccupied during the day and are often restless at night. While occupied they are able to function reasonably well, but the span of attention is limited. In some instances a condition of frank narcolepsy may exist. Factors important in the pathogenesis of this somnolence are not well defined. In our experience it is not necessarily associated with hypercapnia or anoxemia, although the former may play a role in some cases. It is possible that the somnolence is related to a chronic state of fatigue occasioned by the tremendous additional weight which must be carried.

Easy *fatigability* is common. These patients have a decreased work capacity and appear chronically tired. It is probable that the energy exerted in moving the additional weight is so great that the skeletal muscles are constantly fatigued even at rest.

Swelling of the legs is frequent. Although it may be associated with local subcutaneous accumulation of fat or venous stasis and varicose veins, it is well to remember that heart failure may be playing a predominant role. Pedal edema may appear only at the end of the day or may be constantly present. It usually responds favorably to weight reduction and to measures directed toward alleviation of congestive heart failure if this be present.

It is well recognized that in some severely obese persons there is a tendency toward *polycythemia*. Although very high hematocrits have been reported with obesity, in our experience it is unusual for the hematocrit to be over 50% and most of our patients have had normal or high normal values.

In many extremely obese persons one can find some evidence of *heart failure*. The dyspnea or orthopnea may actually represent left ventricular failure and when dependent edema appears in the lower extremities, increase in venous pressure is usually found. Hepatomegaly may be difficult to demonstrate by physical examination but occurs and

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gives rise to mild changes in liver function tests. Distended neck veins will be evident as the right heart fails progressively.

In those patients who remain only partially compensated for long periods we have observed the occurrence of *ocular protrusion* thus giving in some cases a facial stare or "frog-eyed" appearance. Quite commonly one sees an associated conjunctival injection in one or both eyes. There appears to be relief of these eye signs with weight reduction.

Although arterial blood gas studies frequently show some degree of anoxemia, gross *cyanosis* on inspection has not been present in our experience unless there is evidence of congestive heart failure. The cyanosis may become apparent only with exertion or it may be present constantly until congestive heart failure is relieved.

Cheyne-Stokes type of respiration with obesity has been described recently by Isenschmid and associates.[1] In our experience this has been pronounced only in the presence of heart failure with obesity. In another type of breathing seen with obesity there may be apnea of ten to twenty seconds followed by a sudden large gasp with subsequent respirations of decreasing depth until apnea again supervenes.

These are the signs and symptoms we have observed most commonly. There are others which may be mentioned in passing such as aching of back and joints, plethoric facies, gas and epigastric distress.

As a representative case illustrative of the clinical picture of extreme obesity and some of its physiologic consequences, we have selected the following case.

Case Report

A 38 year old negro male truck driver was admitted to the hospital in September, 1957, with congestive heart failure.

Physical examination revealed a B.P. of 180/90 mm. Hg., P. 136 and regular, R. 36 and labored, and T. of 104°. The patient was a well-developed, obese, somnolent colored man weighing 298 lbs. and in acute respiratory distress. The height was 5 ft. 10 in. The skin was warm, moist, and elastic. The eyes had a proptotic appearance. The pupils were equal. There was no frank papilledema on funduscopic examination, though the disc margins appeared blurred, with minimal narrowing of the retinal arteries without hemorrhages or exudates. The pharynx was injected. No distention of the neck veins could be detected with certainty. The chest wall was obese and symmetrical. The lungs had decreased breath sounds and inspiratory and expiratory rales were heard throughout both lung fields. The heart seemed enlarged to percussion though its borders could not be defined well. The pulmonary second sound was accentuated. No heart murmurs were heard. The abdomen was massively obese and no organs could be palpated through the fatty abdominal wall. There was no evidence of ascites. Moderate pitting edema of both extremities was evident.

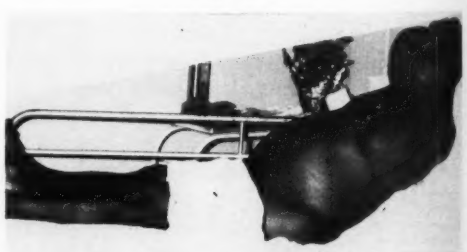
Laboratory studies revealed a Hgb. of 14.6 Gm., a Hct. of 46%, and a WBC of 11,600, with 64 polymorphonuclears, 28 lymphocytes, 7 monocytes, and one eosinophil. The urine specific gravity was 1.025; there was a 2+ albuminuria with 30-40 WBC, and 6-8 RBC per hpf. Serum electrolyte studies revealed: sodium 136, chloride 84, and potassium 4.9 mEq./L. The venous CO_2 was 80 vol. per cent. Sputum culture grew out an almost pure culture of pneumococcus. The admission chest film demonstrated moderate congestion bilaterally. The EKG showed normal sinus rhythm with a tendency toward right axis deviation.

Figure 1 demonstrates the appearance of the patient on admission. One can see the protuberant abdomen, the somnolent appearance, and the necessity for the cardiac position. He was placed in an oxygen tent and given mercurials, digitalis, a low calorie, low salt diet, as well as antibiotics. Over the next three days his congestive heart failure responded satisfactorily but he was noted to be markedly somnolent. Repeated blood CO_2 determinations were elevated. He was removed from the oxygen tent with marked improvement in his mental state. The temperature elevation, thought to be on the basis of urinary tract infection, regressed in three days. He was able to walk about after the 10th hospital day. He was discharged after the 18th hospital day during which time he had lost 54 lbs. of edema fluid and adipose tissue.

Following discharge he was seen in the clinic and weight reduction to 248 lbs. was accomplished with relief of all evidence of somnolence and swelling of the ankles, and with marked improvement in exertional dyspnea. After several months he was able to resume work without difficulty.

Comment. Table 1 shows the arterial blood gas studies that were done. It will be noted that the O_2 saturation obtained 10 days after

FIG. 1



Appearance of the patient several days following admission. Note protuberant abdomen and somnolent expression.

TABLE 1

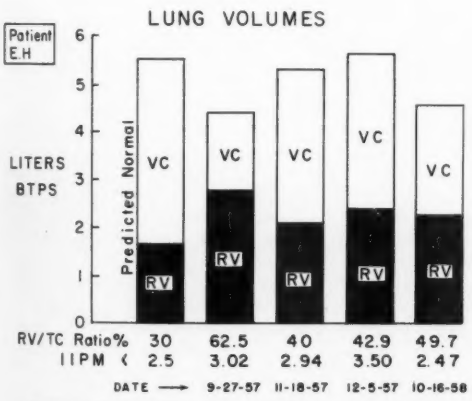
ARTERIAL BLOOD GAS STUDIES

Patient E.H.	*Normal*	*9-27-57*	*Date at Hospital 10-2-57*	*11-18-57*	*12-5-57*
O_2 Sat (%)	96	79.4	86	91.3	78.3
pCO_2 (mm. Hg.)	40	65.6	42		50
pH	7.40	7.38	7.41	7.32	7.36
Hematocrit %	45	47	42.3	45.5	46.6
Weight (lb.)	158	265	258	258	252

admission was still markedly decreased. Over the next 2 weeks there was a rise toward normal to 91.3 per cent. The initial CO_2 tension was high and subsequently fell. No significant change in the hematocrit was found. The pH studies revealed a moderate acidosis which persisted despite a diminution in CO_2 tension. Figure 2 shows the lung volumes as recorded on four occasions. Of interest is the grossly decreased total lung capacity 10 days after admission. One observes that the residual volume is elevated abnormally and the residual volume/total lung capacity ratio is 62.5. Subsequently the total lung capacity was found to be within normal limits and the residual volume still to be somewhat high.

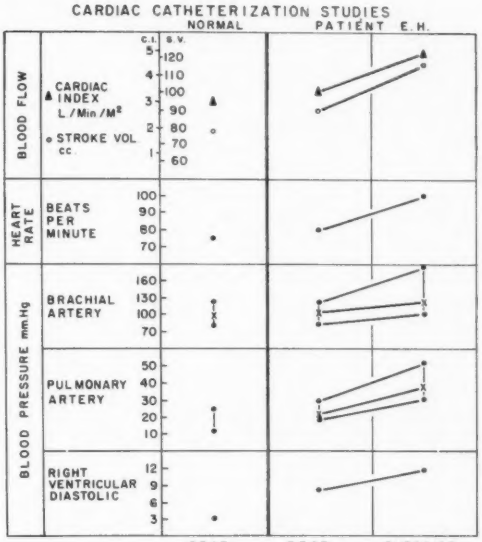
Figure 3 summarizes findings obtained at cardiac catheterization. In the first column are shown the normal values for the various parameters listed on the chart. In the second column are the findings for the patient in the resting state, and the third column data obtained on exercise. One observes that the cardiac index, which is the cardiac output expressed per square meter body of surface area, is normal at rest and rises normally on exercise. The same is true of the cardiac stroke volume. Heart rate was not increased at rest and on exercise shows a moderate elevation. Brachial artery pressure was 125/75 at rest and rose somewhat on exercise. The pulmonary artery pressure was only slightly elevated at rest, but during exercise rose to 52/27 mm. Hg. The right ventricular diastolic pressure is elevated both at rest and during exercise.

FIG. 2



Changes in lung volumes and intrapulmonary gas mixing in patient E. H. with weight loss over a one year period.

FIG. 3



Hemodynamic observations in patient E. H. at the time of cardiac catheterization.

It may be concluded that at least during exercise there is an increased pressure in the pulmonary circulation. Whether this represents a failing left ventricle with secondary increase in the pulmonary artery pressure or abnormality of the pulmonary vascular bed itself is not clear from these data alone. The increase in right ventricular diastolic pressure suggests failure of this ventricle.

Summary

We have described the frequently encountered signs and symptoms in extreme obesity and have shown some of the physiologic effects on the lung volumes, arterial blood gases, and cardiac function both at rest and during exercise. These abnormalities may be partially or completely corrected by weight reduction.

Reference

1. Isenschmid, Van H., Bühlmann, A., and Schaub, F.: Die Lungefunktion bei Adipositas, Helvet. med. acta 2:82, 1957.

Discussion (Abstract)

Dr. John Seabury, New Orleans, La. Physicians are as susceptible to the dramatic as any other group of people. A catch phrase can do wonders in the popularization of a pedestrian subject. Celiac disease comes to life when it is spoken of as "big bellies, flat fannies, and stinking stools." Alveolar hypoventilation is in a somewhat similar category. Alveolar hypoventilation with its consequent hypercapnia and hypoxia has been a frequent problem to the anesthesiologist and those caring for paralytic poliomyelitis. However, it has never been a popular medical subject until its occurrence in some very obese individuals was termed "the pickwickian syndrome."

This syndrome has been very well delineated by Drs. Cole and Alexander. The similarity of this illness to the diabetes of obesity has been noted in that each should correct itself with reduction in weight alone.

I would like to emphasize that the popularization of this syndrome has led to more concern with some of the problems that have been raised by the delineation of this clinical picture. Why does hypoventilation develop in some obese people and not in others who are equally obese? What are the reasons for, and is there any etiologic significance, in the associated symptoms of somnolence, periodic breathing, and polycythemia? I would like to take a few minutes to show how much of the pathogenesis of the pickwickian syndrome has been learned from studies of man in space.

Fat is an unyielding tissue and, if relatively heavily distributed over the lower thorax and abdomen, may mechanically reduce ventilation considerably, the alterations being quite similar to what may be produced by the inflation of an antigravity suit over the lower half of the body. In both instances the minute alveolar ventilation, expiratory reserve volume, and maximum breathing capacity are reduced. The inflation of such a "g-suit" produces an increase in the pulmonary arterial pressure. This also may be observed in some pickwickians. It has been shown that all these abnormalities in the ventilatory volumina can be abolished by weight reduction alone.

Another greatly discussed feature which is present in many of these individuals is the reduced sensitivity of the respiratory center to changes in carbon dioxide. There has been a real problem involving the initial development of hypercapnia. For example, some of these people have been shown to be perfectly capable of fully oxygenating their blood by voluntary deep breathing. Why, then, is the hyperventilation necessary to maintain a normal carbon dioxide level not forthcoming? Is it something related to the work of breathing and perhaps the gradual alteration of the sensitivity of the respiratory center during periods of sleep? Do we have any leads?

It has been shown that the sensitivity of the *normal* respiratory center to changes in arterial carbon dioxide tension is greatly decreased by increasing the work of breathing by artificially produced obstruction of the airway. Drs. Cole and Alexander have pointed out that some degree of airway obstruction is a feature of the pickwickian syndrome, and airway obstruction occurs when the antigravity suit is inflated about the lower body. This experimental work has shown that the ventilatory response to carbon dioxide falls as does the maximum breathing capacity. Consequently, we have at least a possible explanation for the early development of reduced sensitivity of the respiratory center in these individuals.

There is one other feature of the pickwickian syndrome which can probably be explained on a purely mechanical basis. It has been noted that most of these individuals have cyanosis. It has already been stated that some of them can fully saturate their blood by voluntary hyperventilation. However, some of these patients have failed to come to full oxygen saturation while breathing 100% oxygen, although this defect is not present after weight reduction. Therefore, it would appear that right to left shunts are present, and that these must be within the lung and probably of a functional nature, and so disappear with weight reduction. This is not present in all pickwickians. Lewis, Forster, and Beckman have pointed out that applying pressure to the lower half of the body with a "g-suit" not only reduces all of the lung volumes as previously discussed, but results in apparently "trapped gas." This apparently "trapped gas" represents regions of the lung which either are poorly ventilated or do not communicate with the airway at all. This also results in decreased lung compliance, both effects probably being due to the selective "collapse" of the small alveoli. We know that these alveoli are not being ventilated. It is quite possible that continued perfusion of excluded areas of lung is responsible for the functional shunting demonstrated.

CASE REPORT

Hydatidiform Mole: A Review of the Diagnosis, Management and Follow-up—and Choriocarcinoma

A. S. GOSS, JR., M.D., *Jacksonville, Fla.*

RECENTLY I WAS CONFRONTED with a young mother of two children who was definitely not through with her family and who faced the problem of a possible hysterectomy because of a molar pregnancy.

A careful review of the literature on hydatid mole and choriocarcinoma with an outline of a proper follow-up resulted.

It seems worthwhile to record this case and give a brief review of the literature.

Case Report

Mrs. G. G., a 26 year old, G-3, P-2, A-0, white woman had her last menstrual period on Dec. 16, 1955. When first seen on Feb. 28, 1956, she was complaining of amenorrhea of 10 weeks, vaginal spotting for the past 2 weeks, and nausea and vomiting for one week.

Her past history revealed 2 previous normal pregnancies, the last in 1954. She had an appendectomy in 1952; she had had bouts of colitis for the past 9 years. Her menstrual history was normal.

On examination she was an asthenic, well developed, white woman in no distress, but apprehensive and anxious. B.P. was 120/80, P. 90, and weight 110 lbs. Hgb. was 11.5 Gm. Pelvic examination revealed a normal pelvis except for a cervix which appeared typical of pregnancy and some old blood in the vagina. The uterus was enlarged to the size of a 12 to 13 weeks pregnancy (10 weeks pregnancy by history) and was nontender.

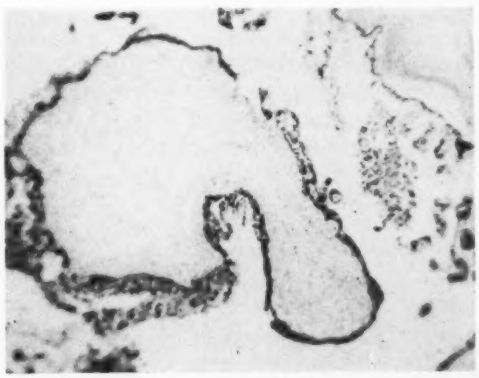
Course. Bleeding became more active and on March 1, she was placed on bedrest, vitamins, and was given 50 mg. progesterone intramuscularly. Although the bleeding subsided, she was hospitalized 3 days later for observation and determination of gonadotropin titers because the uterus now appeared to be 14 to 15 weeks size. On March 6, the vaginal spotting recurred, and she had a sudden episode of severe, sharp right lower quadrant pain of a few minutes duration. By March 12, her uterus extended to 17 cm. from the pubis (19 weeks size); no fetal heart tone nor polycystic ovaries were felt.

On March 15, she developed fever, became nauseated, and complained of being weak. The Hgb. was found to be 7.5 Gm.; the T. was 100.4°. The uterus was now of 23 to 24 weeks size. She was again hospitalized and transfused with a 1,000 cc. of type O Rh positive blood. A roentgenogram revealed no fetal parts; no fetal heart tones could be heard. Chest x-ray film was negative. She was seen by a consultant who agreed with the tentative diagnosis of *mole* and advised emptying the uterus. Gonadotropin titer was not reported until after the diagnosis was confirmed by passage of tissue.

A Pitocin drip was begun and a definite uterine response was obtained. Bleeding increased markedly and she finally passed molar tissue (Fig. 1). During the next 8 hours of Pitocin the expulsion of tissue and blood continued. The I.V. Pitocin was repeated the following day without further expulsion of tissue.

Because of continued bleeding, anemia, febrile course, and clinical deterioration, it was felt desirable to explore the uterus without further delay. Since the uterine fundus was now of about 22 weeks size (decreased from 24 to 26 weeks size), I elected to do a hysterotomy. On opening the abdomen bilateral polycystic ovaries were noted. The uterine wall was thick with no evidence of extrauterine molar tissue. The uterine cavity contained a surprisingly small amount of tissue which was cleaned out with a sponge stick and gauze covered finger.

FIG. 1



The specimen passed spontaneously and had grossly the characteristic appearance of hydatid mole. This shows the characteristic enlarged, edematous villi, with trophoblastic proliferation. (X 72)

FIG. 2

From a specimen passed spontaneously 3 days after that shown in figure 1. There is much greater variation in the size of villi, some of which are not well formed. However, the pattern falls well within the category of benign hydatid mole. (X 72)

On the 2nd postoperative day she passed further molar tissue which microscopically was much more active than any previous tissue (Fig. 2). Convalescence was uneventful and the patient was discharged on the 6th postoperative day.

On April 4, 3 weeks postoperative, she began to bleed profusely. Examination revealed the uterus to be the size of a 6 to 8 weeks pregnancy; the cervical canal admitted one finger and was soft and pliable. Suction curettement revealed "pregnancy effect" in the endometrium but no molar tissue. The patient was given testosterone parenterally. On April 15, and again on May 15, a pregnancy test was negative. The uterus continued to involute, but much more slowly than following a normal pregnancy or abortion.*

Incidence

The incidence of hydatidiform mole varies between 1 in 2,000 and 1 in 4,000 pregnancies, with a more common figure of 1 in 2,500 pregnancies. The incidence of this disease is much higher in the Philippine Islands and the Orient, where it occurs once in every 200 to 250 pregnancies. Choriocarcinoma is a very rare lesion, representing about 2% of all moles.

Etiology

Hydatid moles are believed to be the result of an abnormal pregnancy resulting in the early death or the complete absence of a fetus, and characterized by a marked overgrowth of the trophoblastic epithelium. Only rarely does a mole accompany a full term pregnancy. In a study of 17,000 deliveries at Johns Hopkins Hospital no viable fetus was found in association with a mole. There is one pathologic entity which may be confused with moles, the so-called transitional mole or hydatid degeneration of a normal placenta. Novak[1] believes these changes to be degenerative changes in the villi and are not hydatid mole *per se*. He believes that about 40% of choriocarcinomas arise from moles, 35% from abortions and 25% in conjunction with pregnancies which are farther advanced.

An interesting theory has been advanced on the etiology of moles. Since choriocarcinomas are seen in the male testicle, apparently arising in the Leydig cells, and since no choriocarcinoma has ever been found in the female, unless accompanied by a pregnancy, it was postulated that perhaps the "Y" chromosome in the male fetus is an etiologic factor. However, Novak[1] in studying 28 cases in the Choriocarcinoma Registry where the sex of the fetus was definitely known found no sex correlation to confirm this theory.

Signs and Symptoms

Generally, a mole is suspected only upon the appearance of molar tissue.

A patient is usually thought to be having a spontaneous abortion and is treated as such. In typical cases a mole may be suspected when the uterus is larger than the estimated stage of gestation, with symptoms of threatened abortion, lower abdominal pain, and anemia out of proportion to the obvious blood loss. Often there is a secondary intrauterine infection. Roentgenogram and auscultation of the abdomen fail to reveal evidence of a fetus, except in the rare instances associated with twin pregnancy. However, a normal twin pregnancy and polyhydramnious must be ruled out. Hyperemesis gravidarum, jaundice, and the appearance of toxemia of pregnancy early in the gestation may be suggestive.

Occasionally large polycystic ovaries may be palpated. The cause of the polycystic ovaries is unknown but they are undoubtedly related to a high titer of chorionic gonadotropin. It is known that normal twin pregnancies may be accompanied by polycystic ovaries, believed to be secondary to abnormally high chorionic gonadotropins which produce luteinization and polycystic ovaries. In some animals and apparently in the human, chorionic gonado-

*She resumed normal menstrual cycles and on Dec. 5, 1958, was delivered of a normal male infant by cesarean section.

tropin causes regression of follicles and prolongation and cystic degeneration of existing corpa lutea. Chorionic gonadotropins first appear within a few days after nidation, and by the thirty-second day of pregnancy reach the minimum level required to give a positive pregnancy test (200 to 500 mouse units per liter). The chorionic gonadotropins then rapidly rise, reaching a peak near the sixty-fifth day when they begin to fall progressively. By the one hundred and twentieth day they have fallen about 1,000 to 10,000 u/liter per day. After delivery, they disappear from the urine in 3 to 10 days. Although chorionic gonadotropin titers may be an adjunct in diagnosing hydatid moles or choriocarcinoma, the concentration observed must be related to the physiologic level and curves. At one time it was felt that a positive pregnancy test on spinal fluid was indicative of mole. However, the blood gonadotropin level in normal pregnancy often is high enough to pass the meningeal barrier and give a positive pregnancy test.[2]

Diagnosis

The diagnosis of hydatid mole, prior to the passage of tissue, is usually difficult. The rapidly enlarging uterus, the presence of polycystic ovaries (50% of cases), the symptoms of a "threatened abortion," fever, abdominal pain, jaundice, and the exclusion of a fetus by x-ray, and the absence of fetal heart tones will suggest a molar pregnancy. Once tissue is available for study, the diagnosis of mole or choriocarcinoma is usually a clinical one confirmed by pathologic findings and follow-up.

Microscopically, one sees marked proliferation of the trophoblastic layers with few or no normal villi. The absence of villi is believed to be a very important point in the diagnosis of the choriocarcinoma.[3] In the benign mole there is absence or scantiness of the stromal blood vessels with stromal edema. Some have thought that the malignant cells were from the Langhan's layer but Novak has been unable to confirm this opinion from study of the material in the Mathieu Memorial Chorionepithelioma Registry.

If on curettage one obtains large masses of anaplastic tissue with few or no villi, choriocarcinoma is very likely. Curetted specimens often contain only degenerating villi with trophoblastic overgrowth. This is highly suggestive of a benign mole. In choriocarcinoma, however, the most important tissue may not be available to the curet and quite often the diagnosis is not made until the uterus is removed. Novak[3] found that in only 16% of the cases of the Chorionepithelioma Registry was a diagnosis made by a dilatation and curettage alone.

Treatment

As soon as a diagnosis of hydatidiform mole is made, the uterus should be completely emptied by medical or surgical means. In cases where the uterus is too large for adequate curettage a hysterotomy should be done.

Complications of the mole are many. The most common ones are anemia, sudden profuse hemorrhage, intrauterine infection, and uterine perforation, with malignancy the most dreaded complication. The latter occurs in 1 to 5% of cases. About 16% of moles, although microscopically benign, are locally invasive and are designated as chorio-adenoma destruens.[3,4] They may perforate the uterine wall, the vagina or peritoneal cavity and give rise to serious hemorrhage.

The histologic picture is so variable that pathologists frequently disagree on the diagnosis. In the cases where the lesion is definitely benign or malignant there is little or no question. However, the intermediate groups pose many uncertainties and the pathologists often disagree as to the proper diagnosis.

Follow-up and Prognosis

The follow-up of these patients is most important from the prognostic standpoint but often proves most perplexing. Following evacuation of the uterus, the gonadotropins should be measured at monthly intervals and one may expect approximately 50% to become negative in 2 months. If the Ascheim-Zondek tests remains positive after one month, or if involution has not proceeded normally or if the bleeding persists, another curettage should be done. If a definitive diagnosis cannot be made, but the symptoms continue and the pregnancy test remains positive, still another curettement should be done 4 weeks later. If the symptoms persist thereafter and/or the patient continues to have a positive test for pregnancy after 3 months time, a

hysterectomy is probably the treatment of choice since this clinical picture is almost invariably due to chorio-adenoma destruens or choriocarcinoma. If choriocarcinoma is diagnosed at any stage, immediate hysterectomy should be done. The question of preservation of the ovaries in the very young patient is difficult to answer. If the ovaries appear to be free of gross disease, they may be left *in situ*. However, in the older patient or in one in whom there is any suspicion of a lesion on the ovaries, they should be extirpated.

In cases where the pregnancy test remains positive after 2 months, there are four possibilities: (1) benign residual tissue remaining in the uterus; (2) persistent polycystic ovaries; (3) choriocarcinoma; and (4) a pregnancy has occurred.

Because a positive pregnancy test compromises the care of these patients, it is very important to instruct them regarding contraception or abstinence. Gonadotropin titers are more desirable if readily available for use.

The common sites of metastases are the lungs, vagina, and brain, with other organs being less commonly involved. A routine search of these areas should be done on these patients.

The presence of metastases usually indicates a bad prognosis with a life expectancy of only 4 to 6 months. However, it is known that benign placental tissue may metastasize to the lungs during the course of a normal pregnancy and that it resolve without incident. There are known instances of metastatic choriocarcinoma which have resolved.

Generally speaking, the prognosis with moles is good, the immediate mortality being less than 1.5 per cent. The incidence of locally invasive mole or chorio-adenoma destruens is 16 per cent.

The prognosis of choriocarcinoma is grave and in the Mathieu Memorial Registry was found to have a mortality of 83 per cent.[3]

Summary

A review of the signs, symptoms, diagnosis, management and prognosis of hydatidiform moles and choriocarcinomas has been presented, and the clinical care of such patients has been outlined.

A case of benign hydatid mole has been presented.

Addendum

Since this paper was written, Li and associates[5] have treated a small group of patients with methotrexate, a folic acid antagonist, with preliminary good results. However, their series was too small to be conclusive at that time.

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Therapeutic Approach to the "Problem Patient" with Urinary Calculi*

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The search still continues for a practical means of preventing the continued formation of urinary calculi. This paper considers in detail what is known about the problem, what is unknown, and the application of present knowledge in an attempt to decrease or abolish this process.

THE ADVANCE OF MODERN MEDICINE has produced no "miracle drug" for the prevention of recurrent urinary calculi. The known factors which predispose to continuing calculus formation include a variety of systemic or metabolic diseases, and local urinary conditions of stasis, infection, foreign bodies and retained calculi. The present review takes up the problem at the point where remedial measures for these conditions are already in effect.

The systemic diseases which result in hypercalcinuria are numerous, exceedingly variable in their symptomatology, and in the mechanisms by which they effect an increase of urinary calcium. The local factors which predispose to crystallization and retention of calculi in the urinary tract are equally as numerous and as variable in their symptomatology. In no other disease is there more common interest for the urologist, the diagnostician, the clinical chemist, the surgeon trained in surgery of the parathyroid glands, the facilities and accouterments of the metabolic ward. Table 1 is a partial list of the disease states in which the incidence of urinary calculi is greater than the population as a whole. The differential diagnosis from the point of view of the urologist has been previously considered.[1] The diagnostic criteria and specific therapy of each disease are recorded in the appropriate references to this table.

An organic matrix is the one structural feature common to all urinary calculi. Universally present from center to surface of every concretion, this architectonic framework serves to maintain microscopic crystals in a cohesive mass.[2] The origin of this mucoid is unknown. Neither is there any method known to prevent the aggregation of mucoid molecules into a matrix, nor to effect its dissolution once it has formed. The completely successful prevention of urinary calculi must, in all probability, await the solution of these problems. In spite of this inability to attack stone formation at its origin, there is much that can be done to reduce the rate of the stone's growth or recurrence, to relieve the destructive effects and symptoms of urinary stasis or infection, and to preserve the renal function.

The currently feasible therapeutic approach

TABLE 1

DISEASES ASSOCIATED WITH AN INCREASED INCIDENCE OF CALCIGEROUS CALCULI

	References
I. ABSORPTION (Intestine)	
Hyper-absorption (excrementitial)	3
Sarcoidosis	14
Milk-alkali (Burnett's) syndrome	8
Hypervitaminosis D	8
II. TRANSPORT (Serum)	
Multiple myeloma	8
Berylliosis	15
Cancer with hypercalcemia	16
Oxalosis	17
III. STORAGE (Bone matrix)	
Paget's osteitis deformans	8
Milkman's syndrome	8
IV. MOBILIZATION (Bone crystal)	
Primary hyperparathyroidism	8
Osteoporosis	8
a. Acute (immobilization)	
b. Senile	
c. Postmenopausal	
Adrenal cortical hyperfunction	8
a. Cushing's syndrome	8
b. ACTH or Cortisone therapy	18
c. Adaptation syndrome of Selye	8
Cancer with osteolytic metastases	
V. EXCRETION (Renal)	
"Idiopathic hypercalcinuria"	8
Renal acidosis (tubular insufficiency)	8
Acetazolamide therapy	19, 20

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is directed at the reduction of crystalline deposition within calculi. The various crystalline components account for 97% or more of the weight of most calculi. Approximately 95% of calculi contain calcigerous crystals, 4% are of uric acid, and 1% are of cystine origin. The initial step in any planned regimen is a determination of the crystalline composition of the calculus formed by the patient under consideration. This may be accomplished by polarographic (petrographic) microscopy, x-ray diffraction patterns, or chemical analysis of calculi removed from the patient.

One may make reasonably accurate inferences as to the composition of calculi by a combination of observations. The shape, internal structure, and relative opacity of the *in situ* calculus may be determined from roentgenograms of the abdomen. In order of their decreasing roentgenopacity, calcium phosphate (apatite), calcium oxalate, mixed calcium phosphate and triple phosphate, and cystine calculi are all opaque by ordinary roentgenographic technics. The pure uric acid and "matrix" concretions are completely roentgenolucent. Determinations of the urinary pH and examination of the sediment can be of immediate diagnostic significance. Urinary sediment of highly acid urine from the patient with uric acid calculi is often filled with rosettes or single large crystals of "battle ship" configuration and a brick red hue (Fig. 1). The large plate-like hexagonal crystals of "benzene-ring" shape are common in the acid urine of patients with cystine calculi (Fig. 2). Amorphous urates, triple phosphates, calcium oxalate, and other crystal types are identifiable in the urinary sediment, but are so commonly present in health and in various diseases that they lack the diagnostic significance of uric acid and cystine crystals.

The following general measures are grouped according to the therapeutic objectives as they apply to patients with various crystalline types of calculi (Table 2). Therapeutic success in the prevention of recurrent calculi is directly proportional to the individualization of therapeutic measures for each patient.

Prevention of Crystal Formation

A. *Reduction of Urinary Ionic Concentration.*

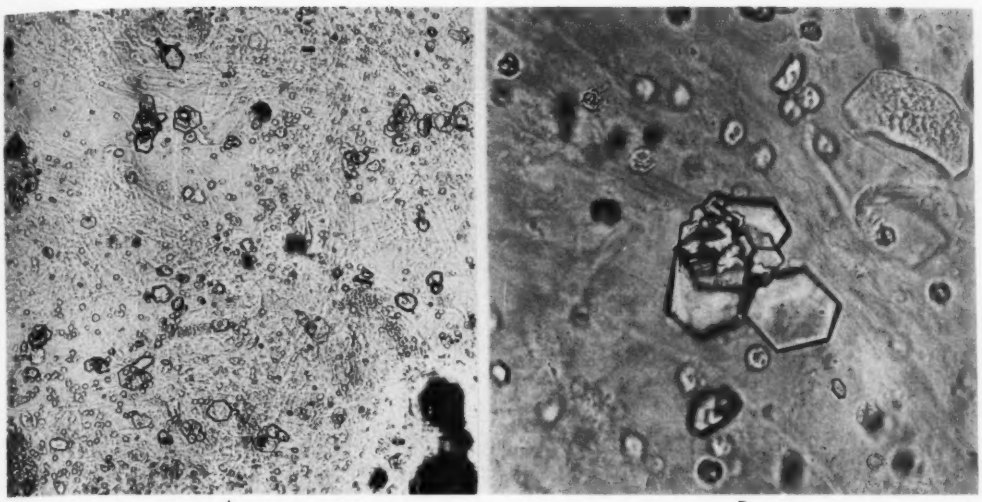
(1) *Dilution.* Diuresis by forced ingestion of water is the universally accepted axiom for prevention of urinary calculi regardless of

FIG. 1

A B

Urinary sediment from patients with uric acid calculi, unstained. (X 400) (A) Rosette formation. (B) "Battleship" configuration.

FIG. 2



A B

Urinary sediment from patient with cystinuria and cystine calculi, unstained. (A) X 100. (B) X 400.

crystalline composition. Distilled water is advocated since any reduction in intake of potential crystal forming ions is desirable. The amount of water intake is gauged by such admonitions as, "drink a gallon of water per day," "keep the 24 hour urine volume at three quarts," or "keep the urinary specific gravity below 1.010." In addition to Ostwalt's dilution principle, diuresis tends to reduce urinary stasis and thereby the time for ion aggregation from less stable to more stable (and usually less soluble) complexes. Maximal urine flow may occasionally induce the spontaneous passage of small calculi.

TABLE 2

I. PREVENTION OF CRYSTAL FORMATION
- A. Reduction of Ion Concentration Per Unit Volume of Urine
  1. Dilution (diuresis)
  2. Reduced absorption
     (a) Depletion diets
     (b) Intestinal binding agents: phytate, aluminum hydroxide
  3. Increased utilization (storage)
     (a) Steroids
     (b) Strontium
     (c) Specific measures in acute osteoporosis with immobilization
        (1) Stimulation of osteoblasts by physiotherapy and estrogens
        (2) Stimulation of bone matrix by androgen, high protein diet, Vitamin C
        (3) Drug and psychotherapy for "alarm reaction"
- B. Addition of Competitive Ions
  1. Nonspecific "common ion" or "salting in" effect
     (a) Hydrogen or hydroxyl ion (pH) effect
     (b) Magnesium
     (c) Urea and other small ions
     (d) Hydrophylic (soluble) colloids
  2. Specific solubilizers
     (a) Citrate
     (b) Glucuronides
     (c) Metal chelate compounds
     (d) Amino acids

II. PREVENTION OF CRYSTAL RETENTION
- A. Prevention of Matrix Formation
- B. Correction of Stasis
  1. Surgery
  2. Ambulation
  3. Diuresis
- C. Removal of "Nidus"
  1. Stone fragments
  2. Foreign bodies
  3. Healthy urinary epithelium (vitamin A)

(2) *Reduced absorption.* The combination of depletion diets and intraintestinal binding agents for crystalline components has the common aim of reduced intestinal absorption and hence reduced excretion of these ions.

Calcium. This alkaline earth metal is the principal cation of fully 90 to 95% of all calculi. Hypercalcinuria is by current knowledge the most common abnormality of the urine in patients with calculous disease, occurring in 70 to 80% of patients with recurrent calcigerous calculi.[3] The majority of these patients appear to be unusually adept at calcium absorption; only a few have renal tubular disease to account for their hypercalcinuria. The reduction of calcium absorption to the minimal amount consistent with a neutral balance is a logical approach to reduced formation of calcigerous crystals in the urine.

The simple admonition to avoid milk,

cheese, and other foods of high calcium content is of *no* practical value to the patient having idiopathic hypercalcinuria.[3] The diet must be specific not only as to the *type* of food permitted and excluded, but also the *quantity*. Thus, approximately 1,900 calories are the maximum obtainable in a balanced diet of 150 mg. of calcium content. This presents quite a problem to the laborer, the athlete, and those with habitual exogenous obesity. Trite as it may seem, many low calcium regimens have ignored the simple fact that an excess of calcium intake may occur with food of even the lowest calcium content, if the "metabolic furnace" is vigorously stoked.

There is considerable difficulty in formulating a diet of low calcium, low vitamin D, and high phytate content from America's processed foods. The practice of "enriching" commercial foods with minerals and vitamins often results in a considerable content of calcium and vitamin D. This is particularly true of cereals and whole grain flour which are the staples of a low calcium diet. Furthermore, the regimen may be surreptitiously defeated by either the patient or the physician. The hypercalcinuric "sun worshiper" must forego the healthy tan. The obese patient must adjust to reduced caloric intake. Commercial vitamin preparations are forbidden, and the physician who prescribes vitamin A must be certain that the preparation does not contain vitamin D also. Medications designed to acidify the urine should contain monosodium acid phosphate rather than ammonium chloride.[1]

Commercially available sodium phytate* is a useful adjunct to the above routine since this material forms an unabsorbable complex with intestinal calcium. It is not a substitute for the most stringent reduction of calcium intake and elimination of factors known to promote intestinal absorption of calcium.[3]

The one indispensable guide to therapy of the hypercalcinuric patient is *periodic determination of the 24 hour urinary calcium excretion*. This should be done two to three times weekly until the patient becomes adjusted to the routine. A satisfactory response is a consistent urinary calcium excretion of 70 ± 20 mg. per 24 hours. Once this has been established the determinations of urinary calcium may be done at intervals of 2 to 4 weeks. Failure to achieve this response with a 150 mg. calcium diet and the equivalent of 9 Gm. of sodium phytate daily requires repeated evaluation of the patient for unrecognized disease involving calcium absorption, storage, or excretion.

Phosphate. In a study of 180 consecutive patients with phosphatic calculi we have not found a single patient in whom the urinary phosphate excretion was significantly elevated above the normal range. In 130 of these patients who had idiopathic hypercalcinuria the mean excretion of phosphorus was slightly less than normal subjects on similar diets. It is unlikely that hyperphosphaturia *per se* is a causal factor in calculous formation.

On the empiric basis that reduced phosphate excretion may reduce the precipitability of urinary calcium phosphate (mass action) Shorr[4] suggested a low phosphorus diet with oral basic aluminum hydroxide gel to precipitate intestinal phosphate as an unabsorbable complex. Favorable clinical results have been reported in those patients who can be maintained on the regimen.[5] None of these reports have included detailed calcium excretion studies. It is well known that urinary calcium falls to exceedingly low values in advanced renal tubular disease and calculous formation usually ceases at this stage of the disease. Periodic determinations of 24 hour excretion of urinary phosphorus are essential to successful administration of the Shorr regimen.

Phytate is the hexaphosphate of inositol and there is usually a marked increase in content of urinary phosphate of patients receiving it. It cannot be administered with basic aluminum hydroxide gels since the net effect of these two substances results in neutralization of the desired effect of either.

Oxalate. As in the case of phosphorus there is no convincing evidence that hyperoxaluria is a common cause of oxalate stone formation.[6,7] Low oxalate diets may serve to reduce the source of exogenous oxalate but they may increase calcium absorption, and they have little effect on the total urinary excretion of oxalate. The low oxalate diet alone is of little value in prevention of calculous formation.

Cystine and uric acid. Classical cystinuria is a genetically determined defect in renal tubular transport of ornithine, cystine, argi-

*RENCAL provided through the courtesy of Dr. Douglas B. Remsen, Squibb Institute for Medical Research, New Brunswick, N. J.

nine, and lysine. In homozygotes there is increased excretion of all four of the above amino acids and, indeed, the clearance of cystine in these persons has been measured at about thirty times that of the normal, a value which approximates the estimated glomerular filtration of cystine. In heterozygotes the reabsorptive capacity for these four amino acids is limited but not abolished, and arginine and ornithine are reabsorbed preferentially to cystine and lysine. Calculous formation in these individuals is much less frequent than in the homozygotes. In theory depletion diets low in these four amino acids and also in methionine should reduce the excretion rate for cystine, particularly in the heterozygote patient. Although the clinical results with such diets have not completely prevented calculous formation in cystinuric patients we have continued to utilize them as adjuncts to the alkalinization and forced fluid routine.

The low purine diet is recommended for patients with uric acid calculi unless the general nutritional state of the patient is such that this restriction is contraindicated. This is not a substitute for the alkalinization and diuresis commonly prescribed for these patients.

(3) *Increased utilization of crystallizable components of calculi by metabolism or storage.* This intriguing concept envisions methods whereby crystalline components of calculi may be diverted from existing normal or abnormal metabolic pathways to other metabolic routes which will prevent urinary excretion of the crystalloids either by storage or by conversion to some noncrystallizable metabolite.

Steroids and strontium. At the present time this concept has practical application only in the steroid and strontium therapy of Shorr[7] as applied to the remineralization of bone in patients with postmenopausal osteoporosis or that due to immobilization. These patients occasionally form calcigerous urinary calculi and such therapy appears to have a beneficial effect in the prevention of recurrence of the stone formation. Strontium salts are much more soluble than those of calcium and there appears to be little danger of the formation of strontium stones.

Since strontium shares many, if not all, of the metabolic pathways of calcium it was considered that addition of strontium to the diet of hypercalcinuric patients might "flood" the absorptive mechanism for calcium with the more soluble strontium. Thirty-three patients with recurrent urinary calculi received 6 Gm. of analytical grade strontium lactate* daily for 17 to 31 months. There was no significant reduction in the rate of stone growth or recurrence in these patients. Analysis of calculi subsequently removed from 5 of these patients revealed only trace amounts of strontium in 3 of 8 calculi.

Specific measures in acute osteoporosis with immobilization. There appears to be a defect in osteoblastic activity due to loss of mechanical stress, hence early physiotherapy and ambulation are recommended in the care of the paraplegic patient. These individuals also have an estrogen-androgen imbalance as indicated by the development of feminine secondary sexual characteristics in the young male paraplegic. Since lack of estrogen promotes a specific defect in osteoblastic activity, small doses of estrogen may stimulate osteoblastic activity in these patients and without side effects if there is associated administration of androgen.

The osteoporosis of acute immobilization is also due to specific defects in the matrix. The loss of androgen, traumatic eunuchoidism, and testicular atrophy of paraplegics may result in a situation indistinguishable from osteomalacia of other causes. This abnormal matrix may also be effected by relative malnutrition, by hypovitaminosis C, and in the extremely agitated patient or one having the "alarm reaction."[8] A complete protein nutritional intake is indicated in spite of the patient's negative nitrogen balance in an effort to provide the full range of amino acid "building blocks" necessary to complete protein nutrition.

Vitamin C should be provided without vitamin D and in large doses since this vitamin may be an active metabolite under the conditions of severe injury and repair. Albright[8] has suggested that the "alarm reaction" of Selye plays an important part in the osteoporosis of acute immobilization. Whatever the mechanism may be, the patient is greatly benefited by the combination of psychother-

*Provided through the courtesy of Dr. Melvin Thorpe, Mallinckrodt Chemical Works, St Louis, Mo.

apy plus physiotherapy and, when necessary, tranquilizing drugs.

B. *Addition of Competitive Ions.*

Nonspecific "common ion" or "salting-in" effect. Crystalline components of calculi pass the glomerular filter in solution. Therapeutic attempts to prevent crystallization in urine have followed the principles of physical chemistry as they relate to the chemistry of solutions. Variation in hydrogen or hydroxyl ion concentration from pH 4.5 to 8.0 is a physiologic property of urine which can be altered by various dietary and medicinal regimens. The solubility of tricalcium phosphate in acid solutions immediately suggested acidification of the urine as a means of preventing precipitation of calcium phosphate. Unfortunately for this concept, urine is far removed from a pure aqueous solution of constant calcium and phosphate composition. The concepts of Raoult, Van't Hoff, and Arrhenius apply to calcium in urine only in terms of the magnitude of interionic attraction as determined by the concentration and valence of *all* charged particles in the urine. Thus, control of the ion activities of all precipitable substances in urine becomes an impossible task, and it is readily apparent that calcium-containing crystals do (and do not) form in urine over an exceedingly wide range of actual calcium concentration. The solubility is determined by the activity coefficient of the involved ions rather than their actual weight per volume concentration.[9]

Clinical failure of the acidifying routines to prevent calculous formation has also been due to other factors. The acid ash diets, ammonium chloride orally, and ketogenic diets usually increase the urinary calcium excretion of both normal and stone forming patients. Cordonnier recognized this and advocated acid sodium phosphate as an acidifying agent for persons with calcigerous urinary calculi. We subscribe to this method of acidification which can be utilized with methenamine in the therapy of chronic urinary infection.[1] The resultant increase in urinary phosphate is not an undesirable development if urinary calcium is maintained at low concentrations by the low calcium, low vitamin D diet plus oral phytate regimen. Acidification of the urine may also be achieved by diets high in cranberry juice or administration of methionine. The former increases urinary excretion of hippuric acid and the latter increases urinary acid sulfate. The effects of these substances on metabolic balance as related to calcium phosphate and other metabolic exchange must await further investigation.

The alkalinization of the urine is a most important phase in the therapy of uric acid and cystine calculi since these substances are much more soluble in urine of alkaline than acid pH. Sodium citrate (Howard's mixture or Citralka) is preferred to sodium bicarbonate. We have observed one patient with cystinuria who developed the classical picture of Burnett's syndrome—hypercalcemia without hypophosphatemia or hypercalcinuria—following 8 years of continued administration of absorbable alkali as sodium bicarbonate. This patient developed progressive renal insufficiency and formation of calcium phosphate stone although she had been free of cystine calculi for 8 years. The urinary pH should be tested on arising and before mealtime. The alkalinizing agent is most effective when taken midway between meals and at bedtime. A supplemental dose may be necessary at 2:00 a.m. if the early morning urine is less than pH 6.8.

Magnesium ions in relatively pure solution are effective competitors with calcium for oxalic acid since the stability constant for magnesium oxalate is 3.4 log $K\triangle$ as compared with 3.0 log $K\triangle$ for calcium oxalate. Hammerstein observed the effect of magnesium ions in preventing calcium oxalate stone formation in rats.[1] This effect can be readily demonstrated by the observation that addition of small quantities of magnesium ions to the Sulkowitz reagent will completely prevent calcium oxalate precipitation. In our experience, the addition of tolerable doses of magnesium citrate to the diet of oxalate stone formers has had no significant effect in preventing stone formation. This result is undoubtedly due to the ionic activities of the involved ions, but modern technology provides no method of measuring activity coefficients of specific ions in urine.

The effect of urea and other ions in making more soluble the crystalline components of calculi has long been recognized and described as the "peptizing" action of urea. This is also a reflection of alterations of ionic ac-

tivity in solutions of various ionic strength. Vermeulen[10] has recognized this in his studies of diffusibility of calcium, but at present no practical applications of this effect are apparent.

The postulation of substances of large molecular weight (hydrophilic colloids) in the urine to increase the solubility of calcium has reappeared in the medical literature for generations. There is no acceptable evidence that any of the nondialyzable components of urine exert a significant influence in the prevention of stone formation by increased solubility of crystalloids. This postulate must remain unconfirmed until more definitive knowledge of the urinary colloids becomes available.

Specific substances increasing solubility. The specific binding of calcium by citrate, glucuronides,[11] amino acids,[12] and metal chelate compounds[13] has been repeatedly suggested as an approach to the prevention of the formation of calcigerous crystals in urine. None of these has proved clinically effective in the prevention of stone formation. Since these substances reach the kidneys by way of the blood plasma they have been exposed to the plasma calcium which is rapidly replenished from the extracellular fluid and from bone. Any substance administered specifically to increase solubility of calcium in the urine may be expected to pass the glomerular filter or the tubular excretory pathways with a full complement of bound calcium at pH 7.4 and under the conditions of specific ionic activity of calcium existing in plasma water. The net effect on urinary calcium is to increase the total quantity with no appreciable effect on the content of ionizable calcium or ionic activity. This has been clearly demonstrated to occur in the case of ethylenediaminetetraacetate. Indeed, this substance binds less calcium as the pH decreases from 7.4 and so may actually increase ionizable calcium in the acid urine when administered intravenously as the sodium salt.

Indeed there may be a specific substance of low molecular weight solubility which provides for increased calcium normally present in urine.[10] If so, it is probably a product of renal tubular transport or metabolism, since this is the only conceivable mechanism by which a calcium-free binding agent for calcium could be presented to the urine.

Prevention of Crystal Retention

All urinary crystals are self-limited to microscopic size and unless bound together can never result in calculus formation. The architectonic substance which accomplishes this is a mucoid matrix. The origin of this material has not been clearly established. There is no information as to the mechanism by which the mucoid molecules become aggregated into a matrix. No method is known by which one may effect its dissolution once the matrix has formed. Prevention of calculus formation may eventually become a reality as information about these subjects becomes available.

The prevention of an aggregation of crystals by correction of stasis recognizes the importance of time in this process. Surgical relief of urinary obstruction, ambulation of the sedentary patient, and the maintenance of maximal volume flow of urine are all important in the prevention of calculous formation.

The role of bodies acting as a nidus in providing a stimulus to deposition of crystals is well known. Retained calculi may be quiescent for years, but they are potential surfaces for increased stone growth at any time. The surgical removal of any calculus too large to pass through the ureter is good preventive medicine.

The role of the urinary epithelium in calculous formation is still unknown and the influence of vitamin A either in excess or in deficiency is a matter of controversy. We have found no "nidus" of epithelial cells, bacteria, or similar formed elements in the many calculi which have been sectioned in our laboratory. A few foreign bodies such as prostatic tissue and catheter tips have been found in large bladder calculi. We have observed no adverse effects from administration of vitamin A but one must be certain that vitamin D is not included in the prescription.

Calcium deposition in renal tubular casts has been clearly demonstrated by microradiography. Whether these are important in calculous formation remains to be determined. We have not recognized casts in sectioned calculi but they would scarcely be detectable in the formed calculus either upon microscopic or microradiographic examination.

The prevention of calculous formation by removal of foreign bodies such as catheters,

sutures, prostatic fragments, and other surfaces for encrustation is too well known to require further comment.

Summary

Present therapy for prevention of calculous formation in the urinary tract is limited to methods designed to prevent crystal growth and retention.

There are many systemic and local diseases of the urinary tract which influence this aspect of the growth of a stone. Practically all of these predisposing influences are subject to counter measures once they are recognized. There is probably no situation that will test the diagnostic acumen of the physician more severely nor demand greater individualization of management than the patient with recurrent urinary calculi.

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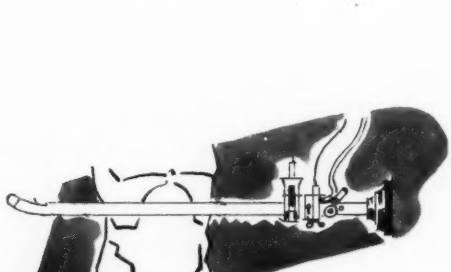

Constitutional Reaction to Penicillinase Used in the Treatment of a Penicillin Reaction*

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This discussion of penicillinase, its indications and contraindications and possible untoward reactions, is most interesting and enlightening.

THE IMPORTANCE OF THE CONTROL as well as the prevention of severe penicillin reactions, which at times may be fatal, cannot be overemphasized. Since the advent of penicillin therapy, we appreciate its therapeutic accomplishments, and the fact that innumerable lives over the years have been saved. We must, along with the desirable features of this agent, recognize the existence of reactions to it.

The control of penicillin reactions, prior to the availability of penicillinase (Neutrapen) was at times most difficult, and the restriction of the administration of penicillin was one of the best preventive measures of a possible reaction.

From the current literature it appears that penicillinase has an outstanding future potential.[1-3] There has been no previous report of antiphylactoid or constitutional reaction following the administration of penicillinase (Neutrapen).[2] I wish to report a case of a constitutional reaction following the intramuscular administration of penicillinase used in the treatment of a delayed serum-sickness-type of penicillin reaction.

Zimmerman[4] has reviewed the various types of allergic reactions to penicillin and stated that antihistamines given concurrently with penicillin may inhibit an immediate anaphylactic reaction, and may mask valuable warning signals of a pending anaphylactoid reaction when the antihistaminic effect wears off.

"Skin testing with penicillin is not of sufficient value to warrant routine use. Severe and even fatal reactions may occur after negative skin testing."[4] When one observes an immediate positive reaction to a scratch or intracutaneous test, this may be considered indicative of a hypersensitivity and is a definite contraindication to penicillin therapy.[5,6]

The Types of Reactions to Penicillin[4]

1. *Delayed reaction.* This simulates a serum-sickness-type of reaction with urticaria, fever, and joint involvement. The incubation period of this type of reaction usually varies from 7 to 14 days, although a minimal incubation may be but a few hours and the maximum up to 8 weeks.

2. *Accelerated and immediate reactions* are rather common and occur only if the patient has had a previous sensitizing exposure to penicillin. Usually there is no previous clinical history of a reaction. The incubation period varies from 5 seconds to an hour, or up to 1 to 2 days. The reaction may be of a severe explosive type; this type of reaction is estimated to have caused 1,000 deaths in the United States.[7,8]

3. *Hyperergic reactions.* These vascular or visceral phenomena are instantaneous types of reactions. They follow the above types 1 and 2 reactions. Some of the lesions may be purpuric, exfoliative, bullous, or there may be an irreversible renal or myocardial involvement.

4. *Erythemato-vesicular or id-like reactions* are found to occur, usually later than the immediate type of reaction, and are thought to represent an activation of silent presensitization induced by previous fungal disease of the skin.

5. *Contact eczematous dermatitis.* This is the typical contact type of reaction with vesic-

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ulation usually at the site of contact, and may usually be confirmed by positive patch-test. Occasionally, exquisitely sensitive patients may have systemic reactions following such contact exposures.

Penicillinase (Neutrapen)

Penicillinase, an enzyme that hydrolyses and inactivates penicillin, is formed by various bacteria (staphylococci, *Esch. coli,* and *B. cereus),* and previously has been used only in bacteriologic media *in vitro* to inhibit penicillin in body fluids to be cultured.[1] Penicillinase has been used in both animals and in man for the inactivation of aqueous crystalline penicillin and procaine penicillin in both oral and parenteral forms. Penicillinase is specific for penicillin, usually inactivating it within an hour after an injection and continuing from 4 to 7 days.[9] Neutrapen may be given in cases of anaphylactic shock intravenously as soon as possible along with other supportive measures. Intramuscular administration is indicated in the delayed serum-sickness and urticarial types of reactions, and in dermatoses secondary to penicillin. It may be given along with other therapeutic agents, such as steroids and antihistamines, to hasten the alleviation of established manifestations of penicillin allergy. The dosage recommended is 800,000 units supplied in a single dose vial as penicillinase; it is supplied as a lyophilized powder to be reconstituted with 2 cc. of sterile distilled water and is then ready for injection as an isotonic solution.[2] The administration of the drug is indicated as soon as possible after signs and symptoms of a penicillin reaction; the dose may be repeated at 3 to 4 day intervals and rarely is a third dose required. Side effects reported by Becker[1] include pain at the site of injection, transitory chills after an injection, associated local erythema and, in one instance, the patient had transitory chills for three hours following this intramuscular treatment. Chills and fever have been reported in some instances following the intravenous use of penicillinase.

Contraindications to penicillinase include: (1) instances where the antibacterial effect of the penicillin is still necessary; (2) penicillinase should not be used if there is no definite indication of the presence of penicillin, since it has no effect on any other known substance; and (3) when a patient gives a history of a previous reaction to penicillinase it should not be given.

Indications. (1) Penicillinase is indicated prophylactically when certain drugs, serums, and vaccines, notably poliomyelitis vaccine,[10] which contains small amounts of penicillin are to be administered; (2) penicillinase may be used in the differential diagnosis of penicillin in the etiology of dermatitis medicamentosa; (3) it also may be used in certain medicolegal differential diagnostic considerations coincident to the administration of penicillin in a known penicillin sensitive patient with a resultant reaction;[4] and (4) for the treatment of allergic penicillin reactions. This would include also the less common reactions of penicillin sensitivity including acute renal insufficiency.[11]

Case 1. (No. 16459) M. A. P., a white man, aged 52, reported that he had a respiratory infection, which he termed influenza, starting about January 1. This continued for several days; his son, who also developed influenza, was treated with penicillin. Since his son responded to the drug, the patient discussed with his physician the desirability of treatment with penicillin also, since he had developed "more cold and his influenza was getting worse." He received, on about February 6, crystalline penicillin, and initially tolerated the drug satisfactorily. He gave a past history of having received, during the time of a war injury, penicillin every three hours for several days. This was tolerated well without any reaction of any type.

On February 19, two weeks after the injection of penicillin, he developed scattered urticarial lesions over various areas of his body. They continued daily, were quite pruritic, and widely disseminated. In addition, there were migratory areas of angioneurotic edema, involving the palms, soles of his feet, and brawny areas of edema in the regions of numerous joints, particularly the ankles. The patient was generally miserable, and stated that these lesions would clear in one area and become more pronounced in others. In the 24 hours preceding his first visit to the Clinic, he suffered considerable distress and was barely able to walk into the Clinic with the aid of a cane. During the questioning he was constantly scratching himself, particularly in the region of the left antecubital fossa, and complaining of pain over the joints with intense itching and burning of his skin in general.

Aggravating factors. The patient was conscious that changes of temperature, becoming chilled or coming from outside into a warm room would cause an exacerbation of the urticarial lesions. At times when taking off his clothes, just that amount of chilling would cause an increase of pruritus and further welts. Furthermore, if his feet were chilled they were extremely painful. Walking or exertion exaggerated the symptoms.

Drugs. His physician had treated him with epinephrine initially; this caused some tachycardia and palpitation. Benadryl, 50 mg., was given every 4 hours without benefit. He was treated with Kenacort 4 mg. tablets, one every 4 hours, with a total of 24 tablets within a week. Histadyl capsules offered no response. He also received a prescription for 12 tablets of Hydrocortone, taking 1 tablet q.i.d. He took only 7 of these; there was no response to the steroid therapy. During the few days preceding his coming to the Clinic, he was given Equanil tablets for rest, one tablet a day; these had helped his sleep, and he had had less itching.

The patient gave no history of intolerance to drugs and, as stated above, had received penicillin on various occasions previously without reaction.

Nonspecific factors. For many years the patient has had a dry skin, particularly during the winter months, which has been rather annoying. There had been some chronic desquamation of his hands and he questioned certain soaps as possibly causing this. *Dove soap* was used currently.

Family history. This was entirely negative for any history of allergic manifestations, either maternal or paternal, except for a son with perennial allergic rhinitis and hay fever.

Therapy. The patient was given, as a preliminary measure, 20 mg. of parabromdylamine (Dimetane), intravenously in 10 cc. of normal saline, slowly over a period of 3 to 5 minutes. By the time this injection was completed, the patient said he had no symptoms of drowsiness or itching, and that the joints and areas of edema of the palms and soles, as well as the multiple urticarial lesions, caused him no itching or distress. He was recumbent at the time of the injection, and after a few minutes got up and walked out of the examining room; after reaching the reception room he discovered he had forgotten his cane, which he had needed when he came into the examining room.

His B.P. prior to the I.V. administration of 20 mg. of parabromdylamine (Dimetane, Injectable, Robins) was 120/80 and his pulse rate 78. There were no changes in these following the infusion. Approximately one and a half hours after the patient received the Dimetane, it was decided to give him 800,000 units of penicillinase (Schenley's Neutrapen). This was given I.M. in the left gluteal area. There was no immediate reaction of any kind. He waited in the office about an hour, as a safety measure, then went out to lunch and reported back to the Clinic some two hours later feeling "fine." He was still not having any distress from his urticarial lesions although they were still evident.

The patient drove to his residence in a small town, some 60 miles from Richmond accompanied by his son, and reported no reaction. He arrived home about 5:30 P.M., complaining of fatigue and of being hot and then very chilly, and changed his clothes. His face was markedly flushed, as reported by his wife, and she made him a highball of bourbon and water, and he was wrapped up well and sat in a chair. After a period of approximately an hour the symptoms subsided and he ate dinner, having no further distress. The urticarial lesions had disappeared by this time. He slept well during the night, and on the following day took care of his customary routine obligations. However, in the late afternoon, on February 27, he reported a return of further itching. He had distress during the night, and on the morning of February 28, he again had an exacerbation of the areas of edema, involving his palms, soles of his feet, and scattered urticarial lesions more extensively than two days before.

He returned to Richmond unaccompanied. Again, as on the morning of the 26, I gave him 20 mg. of Dimetane Injectable I.V. and again there was no side-reaction or tachycardia, but a complete control of the sensation of itching, pressure and distress, although the lesions did not disappear. He again waited some 20 to 30 minutes while I discussed with my associate the desirability of giving the patient further penicillinase. At the time we did not appreciate that the symptoms he had had the evening before, of chilling and redness of his face were possibly secondary to the drug, since the patient at the time told us that he had gone home and had a highball and his face became red. We assumed that this was vasodilatation, and it was only after I talked with his wife on the telephone that the above definite sequence of events were elicited.

According to the directions accompanying the ampule of Neutrapen, it was recommended that in cases of delayed reactions to penicillin it was preferable to give the drug I.M. rather than I.V. The patient complained of localized soreness in the anterior left gluteal area; nevertheless I felt I should proceed with another I.M. injection of 800,000 units of penicillinase. This was given in the right gluteal area. In approximately 3 minutes the the patient called out, saying, "I believe I am having a reaction." The nurse immediately went to him and placed cold cloths on his forehead. He, on his own accord, got into bed, and when she observed him his eyes were rolled back "and all that could be seen was the white," and he was moaning. I was immediately summoned and found the patient in shock with a pasty appearance and his skin had a gray, cyanotic tinge; he was shaking and perspiring profusely. He retched three or four times but did not vomit. The B.P. could not be elicited and the pulse was barely discernible. He was immediately given epinephrine (1:1,000) 0.3 cc. and oxygen was administered by mask; the foot of his bed was elevated. He gradually showed some response; his pulse came through after 3 to 4 minutes, very slowly. He was then given 7½ grains of caffeine sodio-benzoate I.M. At this time his B.P. showed a systolic level of 60; gradually it rose to 80/55, remaining at this level for some 10 to 15 minutes; it was only after approximately one and a half hours that it finally reached the level of 120/80.

After the patient was showing some response, he complained of severe lower abdominal pain with a sensation of possibly having a stool, although he did not, and neither did he void involuntarily. These pains lasted some 10 to 15 minutes as he was coming out of the acute phase of the shock. After one and a half hours he wished to be propped up in bed but, complaining of feeling dizzy, he was again stretched out in bed where he remained for about another hour or more, and then gradually got on his feet. He went

out to get himself a cup of coffee and a piece of pie; he returned to the Clinic and reported he was a "little shaky." Approximately 6 hours after the injection of penicillinase, he was sufficiently recovered to drive home. I talked with his local physician and found he had had no difficulty in getting home, although he was quite shaky and markedly exhausted. At the time he left the Clinic, I prescribed Dimetane Extentabs, 12 mg.; he remained on this drug, taking one tablet every 8 hours until I saw him on the afternoon of March 3, 72 hours after the reaction. He had only an occasional urticarial lesion, seemed to be feeling quite well, and stated that he was able to assume his usual professional activities.

Comment. It was my feeling that, had this patient not previously received 20 mg. of parabromdylamine intravenously on both occasions prior to the administration of the penicillinase, this constitutional reaction might possibly have been fatal. This belief was further substantiated by reports in the literature regarding I.V. antihistamines of a similar chemical group being given as a preventive measure for reactions to injections of pollens and blood transfusions.

Blood was obtained, the serum and cells were separated so special studies could be undertaken with the assistance of Dr. B. Marr Lanman.[2] He reported they were unable to demonstrate the presence of any antibiotics to penicillinase in the serum of this patient, as shown in table 1.

Case 2. (No. 16508) C. P. G., a 42 year old white man, complained of generalized urticaria with itching, and swelling of joints and a sore throat.

The history revealed that in the latter part of July, 1958, the patient had developed bronchitis accompanied by cough and fever, and received an injection of penicillin by his physician. On August 9, he developed quite severe urticaria and was hospitalized 4 days later from August 13 to 14. During his hospitalization, he received the following drugs: Sol-U-Cortef, I.V., Meticortone, 5 mg., Benadryl every 4 hours, and I.V. 5% glucose, which controlled his acute distress. For approximately 24 hours after his discharge he got along reasonably well, and then developed a recurrence of the swelling of his joints on August 16. The soles of his feet and the palms of his hands were swollen. He had marked general malaise and was having a rather acute distress at the time I first saw him the afternoon of August 18. Three hours earlier he had received 100 mg. of Sol-U-Cortef I.V. and was given 25 mg. of Pyribenzamine I.V. During the preceding 5 days he had taken 5 mg. of Meticorten 3 times a day.

Because of marked pruritus, tender and uncomfortable joints, he was given Dimetane Injectable, 20 mg. I.V. This seemed to offer him almost immediate complete symptomatic relief of the pruritus and painful joints. He was given penicillinase one-half hour later, 800,000 units dissolved in 2 cc. of water I.M. in the hip, along with a prescription for Dimetane Extentabs, 12 mg. to be taken one every 8 hours. Twenty-four hours later the patient had marked general malaise, with persistence of the swollen, painful joints and urticaria, as well as sore throat, and his temperature was 104° F. The B.P. was 120/80 and the pulse rate 100.

He was readmitted to the hospital by his physician and was given 1,000 cc. 10% glucose in saline containing one ampule of penicillinase, 800,000 units. This was started at 7:00 P.M. on August 19, and at 8:00 P.M. the patient became quite nauseated. He vomited and complained of a chill; however, the infusion was not discontinued. The patient was given Dramamine, 15 mg. I.M. and continued to be most uncomfortable the remainder of the night. The following morning at about 11:00 A.M., the patient was given an ampule of penicillinase, 800,000 units, which had been dissolved in 2 cc. of water. This was given through an infusion set which had been set up containing 1,000 cc. of 5% glucose and saline with one ampule of Sol-U-Cortef. Approximately one hour later, after 500 cc. of this infusion had been given, the patient complained of severe pains and a chill. The nurse called the intern to see the patient; he was found having a rigor, covered with a number of blankets, complaining of a severe chill. The B.P. was 118/70, the pulse rate 110, of irregular rhythm, and respirations of 26 per minute. There were no nausea and vomiting. The rectal temperature was 101° F.; the patient was slightly cyanotic. The infusion was discontinued. This reaction lasted approximately an hour. At the time of the reaction, the WBC was 34,350, and a differential count showed neutrophils 87%, lymphocytes 11, and monocytes 2%; the Hgb. was 14.7 Gm. On the following day the pa-

TABLE 1

A STUDY OF A BLOOD SAMPLE OF THE PATIENT FOLLOWING PENICILLINASE REACTION

Serum, (Case #1) (3-3-58) was tested for its immunologic properties[2] by means of:
1. Passive transfer in human skin (Prausnitz-Kustner reaction).
2. Passive cutaneous anaphylaxis in guinea pig (PCA).
3. Precipitation in agar gel (method of Oudin).

Antigens used were: Neutrapen (Lot #75-109 and #75-104); Penicillin G Crystalling (Pfizer).

	Prausnitz-Kust. Reac.[a]		PCA in Guinea Pig[b]		Precipitatione	
	Penicillin	Neutrapen	Penicillin	Neutrapen	Penicillin	Neutrapen
Serum (Case #1) 3-3-58	+	—	—	—	—	—

a = Done in 3 test subjects. The end point of transferred reactivity was found 1:100 in 2 subjects and 1:50 in one subject.
b = Done in 6 animals. 3 were challenged with penicillin and 3 with Neutrapen (Lot #75-109).
c = Done 3 times. Neutrapen used for challenge (Lot #75-109).

tient received 500 cc. of 5% glucose and saline containing Sol-U-Cortef, 100 mg. During the next 5 or 6 days the patient showed progressive improvement, although he continued to be extremely weak. On August 27, the day of discharge, one week after the initial reaction, the WBC was reported as 16,700, with a differential count of neutrophils 61%, lymphocytes 34%, monocytes 3% and eosinophils 2 per cent.

Comment. The symptoms in case 2 were consistent with those of side-reactions described by the manufacturer and included chills and fever. In addition, he had a very irregular pulse. This reaction was not the explosive constitutional shock or antiphylactoid type of reaction that was noted in case 1. The patient in case 2 had immediate symptomatic relief of the itching and painful joints following intravenous Dimetane Injectable, and 30 minutes later was given an intramuscular injection of Neutrapen, 800,000 units. The patient did not experience the chill and other side-effects which followed the intravenous penicillinase, in combination with the intravenous saline and Sol-U-Cortef. It was further noted that there was no reaction to intravenous Sol-U-Cortef, 100 mg. given in an infusion of 5% glucose and saline. Case 2 further reveals that this patient, who had urticaria and a delayed serum-sickness-type of reaction secondary to penicillin, should not have had treatment with intravenous penicillinase. The intramuscular injection of this was followed on two consecutive days by intravenous penicillinase.

Summary

A review of the current literature on penicillinase in the treatment of penicillin reactions was made. The types of penicillin reactions included "delayed reaction," "accelerated and immediate reaction," "hyperergic reactions," "erythemato-vesicular or id-like reactions," and "contact eczematous dermatitis." Indications and contraindications to penicillinase therapy, both by the intravenous and intramuscular routes were commented upon.

Two cases were presented. The first had a severe constitutional or antiphylactoid type reaction immediately following a second intramuscular injection of penicillinase. It was postulated that, had the patient not previously been given parabromdylamine (Dimetane Injectable) intravenously, this reaction might have been fatal. The second case revealed some of the side-effects that have been described coincident with penicillinase therapy.

This report has been made to bring to the attention of the profession the possibility of a constitutional reaction following penicillinase therapy. However, it is not to be inferred that penicillinase should never be given, since it offers a very worthwhile therapeutic response in the treatment of reactions to penicillin.

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Considerations of Autonomic Blockade in General Anesthesia*

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The authors point out that the usual anesthesia merely eliminates painful stimuli and makes the operation easier. However, the authors indicate the role the autonomic mechanism plays in the development of shock. The authors maintain that blockade of the autonomic nervous system reduces morbidity through the reduction of noxious stimuli which are a hazard to the organism which reacts with shock.

ANESTHESIOLOGY, within recent years, is progressing beyond the point of considering the patient's status only during the operative procedure. Rare should be the anesthesiologist who considers his job is done if and when he returns the patient to his bed.

Miller and Johnson[1] have stressed the postoperative pulmonary complications following operation upon patients with uncertain respiratory reserve. They have also devised a simpler preoperative study of pulmonary function together with both pre- and postoperative treatment to aid in this field.

Now, with the increasing numbers and magnitude of surgical procedures being offered patients, it becomes imperative that we consider our technics of anesthesia with reference to the prevention of operative shock and improvement of the over-all postoperative condition.

It would be well to evaluate technics which have been authoritative in the past only because of routine. Boba and Converse[2] have approached the problem of hemorrhagic shock with a plan which is as provocative as it is different from the traditional but often ill-founded utilization of vasopressors.

The purpose of this paper is to present for your consideration the inadvisability of leaving the defense mechanism of the patient intact when this reaction itself has become more injurious to the patient than the aggression which initiated it. Our aim is to discuss the damping out of this mechanism at various levels and to show our reasoning for the belief that this should be performed centrally as opposed to peripherally.

We believe that, by utilization of technics based on these principles, we can consistently ameliorate or completely obviate postoperative shock and aid the patient toward an uneventful recovery from the operative procedure.

Physiologic Considerations

Although it is not proposed to enter deeply into discussion on the condition of shock itself, it is necessary for the clarification of statements which are to follow that the body responses to aggressions be evaluated. All aggressions produce in the body through the mediation of the subcortical system the same reaction, that of vasoconstriction. Depending on the type of aggression, however, this primary mechanism of vasoconstriction may be further complicated. Thus, in hemorrhage there is a further loss of fluids available for circulation, and in gram-negative shock there is an infective process. If this condition of vasoconstriction is maintained, capillary stasis and loss of circulating fluid result as a secondary mechanism, and now the condition of shock is established. Theories are numerous with regard to the cause of "irreversibility," but suffice it to say that if the condition of capillary stasis remains the reaction feeds on itself until circulatory collapse finally ensues.

In normal circumstances the initiating aggression is short-lived and, before harm results from the capillary stasis secondary to the vasoconstriction, the whole reaction dies down spontaneously. Thus, the patient who is essentially normal preoperatively is quite

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able to withstand the ill effects of a brief period of operative shock and, in the long run, is little the worse for it except possibly for an increased morbidity during the postoperative period. The results are different, however, if the operative shock is severe or prolonged, as in major surgery or if the patient is debilitated. Here the state of vasoconstriction becomes well-established, serious shock develops, and the scales may well be turned against the patient.

Though hypotension follows the vasoconstriction and loss of circulating blood volume, this is a secondary effect and is not in itself responsible for the production of shock. Probably because hypotension is the most easily measured effect of shock, treatment has been directed toward rectifying this with the help of vasoconstrictors. Vasoconstriction is the primary mechanism of shock production, however, and the result of such treatment is to increase the condition of shock. A case can be built for directing treatment toward the relief of the vasoconstriction which is, after all, the primary cause. In the prophylaxis against shock it is either necessary to prevent the vasoconstriction occurring by paralysis of the arterioles or to prevent the initiation of the vasoconstrictive stimuli by altering the response of the reticular activating center.

Writing in 1914, on the shock-producing effects of surgery even though the patient be under the influence of a general anesthetic, Crile and Lower[3] stated, "The afferent path from the seat of injury being unbroken, the afferent stimuli reach and modify the brain cells as readily as if no anesthetic had been given." In his concept of anoci association Crile presents a most tenable argument that general anesthesia does little but relieve the patient's conscious perception of pain, leaving the rest of the stimulus and its deleterious effects intact. General anesthesia will not prevent response of the neurovegetative centers to aggressions such as major trauma and blood loss which are visited upon the organism.

Optimism brightened the period when the curariform drugs were introduced into clinical anesthesia, since relaxation then became possible without deep anesthesia calling for large doses of drugs. With light anesthesia it was anticipated that patients should be in a better condition following surgery. Then it was believed that general anesthesia blocked the afferent impulse from the seat of injury, and the deteriorated condition of the patients postoperatively was a direct result of absorption of the large quantities of anesthetics used. A little more attention to the writings of Crile and we might have been spared the disappointment which was to follow. Crile had stated that it was only in the protection against psychic strain that there was any difference at all between the patient being made compliant for surgery by general anesthesia or by paralysis with curare. Certainly, with the use of curare the anesthesiologist was able more easily to produce excellent working conditions for the surgeon, and because of this there was some improvement in the postoperative condition of patients. The gentler handling of the tissues as a direct result of the greater accessibility resulted in some reduction of the aggression to the patient.

Use of Hypotension

By 1952, the clinical observation was being made that patients undergoing operation under "controlled hypotension," using the methonium compounds, were in a physiologically better state following operation than one would have reasonably expected. In many medical centers results were sufficiently consistent with this technic to make a very definite good impression. Little,[4] in his excellent treatise, states, "One interesting outgrowth of the use of controlled hypotension in anesthesia and surgery has been the use of ganglionic blockade to prevent the transmission of noxious impulses. This is not, of course, a true indication for induced hypotension itself, but it has been suggested that the future may prove the usage of ganglionic blockade is the most important and enduring contribution that the technics of controlled hypotension have made to medicine." This method of protection from shock was not, however, generally explored further and was not likely to be, so long as the conflict raged with regard to the morality of the utilization of controlled hypotension. Particularly was this so since the very patient on whom it would be desirable to use some preventative method against shock would be the one to show most of the accepted contraindications to hypotensive technics.

Interest in the subject of prevention of shock was stimulated for one of us (D.C.) some eight years ago by work in the original Center for spinal injuries at Stoke Mandeville Hospital in England. It had long been noted at the Center that patients with complete cord injury, especially those with cervical and high thoracic damage, suffered from intense vasomotor collapse following operation. Certainly, this vasomotor collapse was quite independent of the blood loss. Further, these same patients, because of the nature of their disability, returned repeatedly to the operating theatre for various genitourinary and plastic operations. With such a schedule of repeated operations, the patient's reaction to operation became familiar. He could serve as his own control in the determination of the effectiveness of prophylactic measures against postoperative shock.

In this hospital the usual patient with a complete cord lesion could feel nothing of the operation. From this point of view, general anesthesia was unnecessary. However, without general anesthesia, it was noted that most patients became very uncomfortable during the procedures, often complaining of pain and referring it to the site of their cord lesions. Either with, or without general anesthesia vasomotor collapse soon became established and remained so for several days following the procedure, in spite of treatment along generally accepted lines. Because of the failure of vasopressors and transfusion to assist in the treatment of this condition, a new approach was sought. In 1951, on the grounds that histamine might in some way be connected with the initiation of shock, oral and intravenous preparations of antihistamines were used both for attempted prophylaxis and treatment. The results, though not consistently good, at least showed some success which had been absent with the methods of treatment used up to that time. In retrospect, of course, it will be realized that the partial success of this as a form of treatment was due to the effect of the antihistamines toward preventing or relieving the vasoconstriction.

Later in 1951, controlled hypotension came into use for specific cases, notably for those having renal operations, and in whom it was desirable to reduce blood loss to a minimum. These same patients who had been such a postoperative problem before, now recovered from their induced hypotension over the few hours following operation but now without the occurrence of shock. Since this time, in selected cases, the methonium compounds have been used deliberately to reduce postoperative shock and the concomitant controlled hypotension has been accepted as a calculated risk.

Since hypotension of some degree must necessarily follow both ganglionic blockade or its extension into complete autonomic blockade, it is necessary to be perfectly clear that the terms "hypotension" and "shock" are not synonymous. The hypotension which is present in vasoconstriction and the condition of shock is the result of loss of circulating blood volume. The hypotension associated with autonomic or ganglionic blockade and vasodilatation is due to a lessening of peripheral resistance and an easier circulation of the blood. Both clinically and experimentally, it has been shown that the arterial blood pressure and tissue flow may have no direct bearing upon one another. The pressure in any artery is the resultant of two factors: the minute volume of blood flowing into that artery and the peripheral resistance beyond the point at which the pressure is being measured. This peripheral resistance resides mainly in the arterioles and probably to a lesser extent in the capillaries and veins. In the individual who is erect and about his daily work, it is necessary that a certain head of pressure be maintained within all the arteries to insure a satisfactory distribution of the circulating blood about the body. In a recumbent, premedicated or anesthetized patient, however, the problem of distribution is easier, and it is conceivably to his advantage that the back pressure against which the blood is being pumped should be lowered. If the minute volume of blood entering the artery is unaltered, this lowering of resistance to flow will result in a lowered arterial blood pressure. Under these conditions hypotension is not dangerous for there is a significant decrease in the work load on the heart and the blood flow through the vital organs is unchanged. This state of affairs is quite the opposite of hypotension or even the maintenance of a normal blood pressure in the face of active vasoconstriction when the work load on the heart is increased

and the tissue flow is minimum. The concept of tissue flow is the important consideration. To maintain blood pressure at a considered normal by effecting vasoconstriction, which can do nothing but reduce tissue flow, is deserving of some critical consideration.

It is of equal importance not to give the impression that hypotension itself is a necessary part of the prophylaxis against shock. Prevention of shock is brought about by the prevention of the primary causative mechanism of vasoconstriction. It is the means used to this end, ganglionic or autonomic blockade, which may produce hypotension as a secondary effect of the vasodilatation.

There is a rationale for the use of technics to prevent the normal reactions of the body to aggressions. These aggressions set off in the body a series of neuroendocrine reactions called "defense," the most important of which is vasoconstriction. The reactions tend, for a time, to conserve homeostasis and to protect the individual against the effects of the aggression. If, however, the aggressions are severe or prolonged or the individual debilitated, the defense reactions go on to cause capillary stasis and shock which become more harmful to the patient than the aggressions themselves. Thus, it may be the reaction of the patient which leads to a progressively worsening status. Logically, therefore, it would be reasonable to damp out this reaction to protect the patient from the ill effects which must otherwise follow.

In its early stages of reaction to aggression homeostasis correctly describes the task which is performed by the defense mechanism, but as the condition passes on into shock the stability of the organism is destroyed by the reaction. One cannot stress too often the fallacy of attempting to preserve homeostasis only by the utilization of vasopressors to maintain the blood pressure measured at the brachial artery at the expense of the organism as a whole. Converse,[2] in his review on the treatment of shock with ganglionic blocking agents, shows by theory and experiment that the use of vasopressors with nothing in mind for treatment other than the maintenance of blood pressure is doomed to failure. This form of treatment will increase the condition of shock by a further increase of vasoconstriction and may, in all probability, accelerate the death of the patient.

Prophylaxis of shock by the use of ganglionic blockade is a comparatively simple procedure. However, the treatment of established shock by this method, and especially hemorrhagic shock associated as it is with fluid loss, though theoretically correct is difficult to practice and fraught with danger. The use of the ganglionic blocking agents in relaxing the constricted arterioles tends to give rise to further immediate fall in the circulating fluid volume before making the blood lying dormant in the capillaries available to the circulation. In practice, autonomic blockade is the easier method to use. In this case, the arterioles are not directly paralyzed. Rather the vasoconstrictive stimulus is obtunded centrally so that the vessels slowly return to an almost normal state. The capillary stasis is relieved at the same time, and the volume of fluid available for circulation is increased along with the increase in circulatory volume.

"Autonomic Blockade"

The preferable technic by which the condition of shock is prevented from arising is by a controlled inhibition of the autonomic nervous system in such a way that the initiation of the vasoconstrictive impulse is precluded. For, in the use of this method, the hypotension is of a very much less order than it is in ganglionic blockade. This technic has come to be known as "autonomic blockade" and it calls for a complete block of all the defense reactions of the autonomic system. It is unfortunate that there is no one drug available which is capable of producing this effect and for this reason, the technic calls for the use of several drugs at the same time. The polypharmacy of some of the earlier workers has been avoided, however, and one is striving toward simplicity with the technic.

In the light of the work of Magoun and Morruzzi[5,6] on the reticular activating system, it would now appear probable that the autonomic block is produced centrally in this region and not at various points in the periphery as was previously believed. We think that "reticular blockade" might now be deemed to be a more satisfactory term for this technic because the reticular activating system is the probable site of this blockade. Under the circumstances, it would be well to touch on some of the main points of the

reticular system at this time. The blockade is effected by the use of phenothiazine derivatives together with meperidine. In order to understand the action of these drugs, some knowledge of the reticular activating system is also necessary.

The reticular system[7] is made up of two parts, the descending and the ascending. The descending system, made up of medial and lateral tracts on each side, affects reflex muscle tone, and the areas from which it arises would appear to be synonymous with various parts of many autonomic and purely self-governing areas, such as the inspiratory and expiratory areas, the vasomotor and the vomiting centers. The ascending reticular system appears in the brain as an ill-defined collection of nerve cells and fibers which receives connections from the spinal and the cranial afferent nuclei involving most of the modalities of sensation. The complete subcortical system, particularly the reticular formation and the hypothalamus, coordinates the visceral, somatic and psychic functions of the brain to cause what we have come to accept as the normal reaction of the body when subjected to an aggression or to a change in its environment. The parasympathetic and sympathetic parts of the peripheral autonomic system are reflected in the subcortical areas by two mutually antagonistic neuromechanisms. These two mechanisms are referred to by Hess[8] as the trophotropic and ergotropic divisions. Stimulation of the trophotropic division integrates parasympathetic and somatic motor activities, to give such reactions as drowsiness and increased parasympathetic activity, decreased tone of skeletal muscle and activity and lowered responsiveness to external stimuli. Ergotropic stimulation integrates sympathetic with somatic motor activities to give arousal, increased sympathetic activity, increased skeletal muscle tone and activity, and activated psychic state. Normally, these two divisions are in a balanced state. The action of drugs in this area is to produce predominance of one or the other system. This may follow either stimulation of that system or depression of the opposing system.

It is probable that the action of chlorpromazine is exerted primarily on the reticular system by depressing the ergotropic division and in blocking the excitant action of the circulating epinephrine upon this system.[9] Other phenothiazine derivatives, such as promethazine, have two probable sites of action: the ascending reticular activating system and the hypothalamus. Thus, in using a mixture of these two drugs, chlorpromazine and promethazine, it would appear possible to produce a very wide block in the reticular system and so prevent the initiation of the defense reaction by paralysis of the mediating center.

Clinically and experimentally, it has been shown that the administration of a mixture of these two drugs, together with meperidine for its action on the cortex, is effective in the prevention of shock following severe aggression to the body. Vasoconstriction does not occur for there is a specific lowering of the pressor response producing relaxation of the arterial and arteriolar tone. The veins are relaxed and well filled with blood, and the capillary bed remains stable.

It might be well to pay more than a little passing attention to the reticular activating system for it may easily be possible that the future of anesthesia lies with drugs which have a specific action at this point. For the introduction of a technic which utilizes such a philosophy we are in debt to Laborit and Huguenard.[10] It is unfortunate that the general acceptance of this technic, however, has probably been delayed by the methods of polypharmacy they used and the early results they published.

Very shortly, the technic consists of the administration of chlorpromazine, promethazine, and meperidine to a patient. Lowering of the body temperature might at times be indicated but it is optional. The pulse rate remains steady after a slight initial rise. The blood pressure falls on an average about 20 millimeters of mercury. The patient remains quiet, relaxed and completely indifferent to the outside world with almost total loss of sensation. He may respond to a very strong stimulus. The extremities remain warm and are a pale pink in color. Respiration is slow and deep. General anesthesia may be induced with nominal doses of chosen drugs.

It cannot be sufficiently stressed that during operation it is essential that the patient's circulating fluid volume be kept up for his compensating mechanism is no longer in action. For the same reason, precaution must also be taken against overtransfusion.

The operative course is generally without complication. Following operation the patient can be aroused by a strong stimulus, auditory or painful, but if left alone will sleep peacefully for a period of some hours. This sleep results from lack of stimulus to keep him awake rather than from drug depression.

The great advantage of this technic, as it has been used up to the present time, is that one is able competently to undertake the anesthetic care of patients who would previously have caused great anxiety or who would have been considered unfit to withstand major surgical intervention. Following operation the patients require less nursing care than normal, and fewer of the postoperative complications which might be expected to follow major surgery are found. Improved drugs which act primarily on the reticular activating system are now being made available for clinical use.

Summary

A case has been presented for the utilization of reticular blockade as the most satisfactory means for the prevention of shock during operation. The results obtained are claimed to be superior to, and more controllable than those which could be achieved by the use of ganglionic blockade. A rationale is developed for the more general use of such a technic to aid patients toward uneventful recovery from operation.

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Discussion (Abstract)

Dr. J. Gerard Converse, Miami, Fla. The approach of Drs. Canter and Jenkins to protection of the patient against prolonged pathologic vasoconstriction by prophylactic "reticular blockade," again focuses attention on the need for careful re-evaluation of time-honored philosophies in medicine. Indirectly at least, these authors also raise the question as to the real importance of maintenance of blood pressure, by whatever means, at so-called normotensive levels, and infer that we as physicians may be treating only ourselves vigorously, occasionally to the detriment of the patient.

Since very little of anything is either all good, or all bad, it might be appropriate to dwell briefly on what I consider to be some of the bad in the environmental dissociation program advocated by the authors.

First, I believe that there are limitations in the area of physiologic old age. The antiquated coronary tree is probably pressure sensitive in that it relies on maintenance of a mean arterial pressure within narrow limits in order to sustain flow—a situation probably quite different from the physiologically young coronary system. The decrease in work of the heart subsequent to decreased peripheral resistance may not be sufficient to counterbalance the deficit in coronary flow secondary to a lowered mean arterial pressure, with a resultant relative myocardial hypoxia.

Second, again focusing on the geriatric group, drug-induced environmental separation, may be additive to the psychic disturbances so common in the aged, who, without any drugs, may lapse into a psychotic state merely from being in a hospital, separated from familiar landmarks. Our philosophy has been one of belladonna (atropine) premedication only in patients over the physiologic age of 65.

Third, the drugs presently available for "reticular blockade," if that is indeed how they function, lack controllability when administered in the usual fashion for preoperative medication. Since they are not rapidly metabolized, they should not be used as "drip medication," since the essence of safe "drip medication" lies in the titration of input against output once the priming dose produces the desired effect. Trimethaphan, on the other hand, has much to offer in terms of controllability since input can be titrated against a rapid rate of destruction. This is important—the controllability of effect—since the stimulus and response pattern of man undergoing surgery is not static, but a dynamic picture demanding a definite elasticity in drug administration.

Fourth, the warning of the authors concerning maintenance of circulating fluid volume, is not an idle one in terms of the bad things that can arise with deliberate vasodilatation. In terms of the possibility of overtransfusion, it might interest you to know that a dog under the ganglionic blocking influence of trimethaphan may be transfused with an amount of blood almost equal to his normal blood volume without showing any of the objective signs of circulatory overload, except for a slowly-rising central venous pressure—not a common clinical measurement in man. Cessation of ganglionic blockade with return of constrictor tone to the vascular bed leads to tremendous venous engorgement, and acute hepato- and splenomegaly as these organs in this species act as tremendous blood reservoirs. In man, whose spleen

and liver probably do not assume this function, fulminating pulmonary edema may ensue. Divorcement of sympathetic tone can thus easily open the way for circulatory overload.

As a final comment in this deliberately unilateral view of "reticular blockade," I note with interest the authors' comment that "following operation the patients require less nursing care than normal. . . ." I might point out that several of the patients, suffering from hemorrhagic hypovolemia in whom we have utilized ganglionic blockade as an adjunct in their therapy, have required no nursing care at all.

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Problems of Nutrition in Industrial Workers*

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For efficiency in industry, the employee must be assured of a satisfactory nutritional state. This is a matter for which the industrial physician has responsibility.

Introduction

WHENEVER WE DISCUSS THE SUBJECT OF NUTRITION, we think in terms of food. Nutrition has been defined as the science of food and the nutrients in food that are necessary for health. It is the science that deals with the physiologic needs of the body in terms of specific nutrients,—calories, water, essential amino and fatty acids, vitamins, and oxides and salts of inorganic elements.

Since all forms of life depend upon food, this should be sufficient in quantity and quality to supply the body with the necessary elements to accomplish its functions,—growth, work, and reproduction. Foods produce calories and they should be in direct proportion to the activities of the man. A laborer will perform his job adequately if he has the sufficient calories required for that job. But, on the contrary, if he supplies his body with insufficient food, thus having a lower intake of calories, he must burn the tissues of his own body for the necessary energy; this, of course, can only be done for a short time.

Failure to supply the body with enough food or some of its components is not the only nutritional problem found in the industrial worker. Excessive eating, with an excess of calories, means the deposition of fat in the body tissues and obesity. Overweight is not an organic disease, but it does predispose the body to diseases. Obesity is associated with the increasing incidence of many serious ailments.

Many obese people are sure their increase in weight is due to endocrine disturbances and not to excessive eating, but it is well known that endocrine obesity is not at all frequent. In most of the instances obesity is due to the natural law of supply and demand; the body has more calories presented to it than it needs, and this excess of food is deposited in the organism in the form of fat.

The increase of the so-called degenerative diseases during recent years, is due, no doubt, to our success in controlling infections. What we have really achieved is a longer age span in our generation; thus more people are arriving to ages where these diseases are more frequently seen.

A great deal has been done to prevent and control degenerative diseases. From a standpoint of industrial medicine one of the first steps should be to make an early diagnosis of these diseases (hypertension, diabetes and atherosclerosis) through periodic examinations. Research and other studies have shown that obese persons are more predisposed to degenerative diseases and that the incidence of their death during the period of productiveness is higher than in other individuals. This explains why obesity is another nutritional problem in industries.

Nutrition in Industry

To determine the nutritional problems in an industry one should focus attention on the following points: (1) observation of the eating habits of the place where the industry is located; (2) knowledge of the foods which are easily acquired in that locality; and (3) study of those foods and the method of preparing them for eating.

With this knowledge one is in a better position to make an individual study of the industrial worker's nutritional status, not with the aid of collective surveys but from each worker at the time of his periodic check-up examination.

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Of primary importance is the detailed inquiry into the laborer's daily diet. To questions on the type of food he consumes, the usual answer will be that he eats well or that he eats a balanced diet, but one should not be satisfied with such answers. He thinks he eats well because he satisfies his appetite. On the other hand, the idea of poor or scanty eating is associated in his mind with "going hungry," a fact he will never confess.

One must also stress the hazards of excesses as well as of deficiencies. The obese person is amazed at his gaining weight in spite of his poor eating, but the results of a detailed inquiry will make note of the difference between his answers and what he really eats.

In our opinion a medical record will not be complete if it does not have a special dietary form to aid in knowing the laborer's eating habits. This is our usual form for recording health inventories, but, as you can see, it leaves very little space for a detailed dieting questionnaire. We have added this special form, which as you can see is divided into three parts:

1. We ask the foods liked, disliked and the ones that do not agree with them.
2. The kind of food eaten at each meal.
3. The amount of each food consumed daily.

Until now we have dealt with the first phase of the periodic health inventory and shall now consider the second phase, or the physical examination. With nutritional problems in mind we should expect to find beriberi, scurvy, rickets, pellagra, and the like, but fortunately, such clinical cases are seldomly found because deficiencies are not so marked as to produce these diseases.

What we see are the subclinical forms, most of them persons suffering from a combination of a partial deprivation of vitamins along with a lack of essential proteins and inorganic chemical substances. The effect of a persistently, slightly faulty diet may not be detectable for years in as much as symptoms are vague and numerous. They may produce changes in the skin and other epithelial tissues, in the nervous system, alimentary tract, hematopoietic and cardiovascular systems, which usually are ascribed to other diseases.

Our Industry

Based on our observations we may say that Cuban laborers in general have a very poor breakfast. Let us consider laborers in our refinery: 65% take just a cup of coffee and milk, and this second ingredient is not of very good quality; about 20% add a portion of bread and butter; only 3% consume a well-balanced breakfast of milk, fruits, butter, cereals and ham or eggs, and the remaining 12% drink exclusively a small cup of sweetened black coffee. With this in mind, consider how well the workers in this last group can do their job after a night of fasting, if they start the day with the few calories contained in a small cup of sweetened black coffee.

A brief analysis of the foods taken by our workers at the refinery was made; the majority eat at home. The dietary deficiencies are self-evident: Consumption of milk and its by-products is very poor. The eating of proteins does not reach the normal level; green vegetables are not used frequently; eggs are not taken in sufficient amount. The basic food is carbohydrate consumed in excessive quantities: rice, grains, sugar and viandas (root vegetables). A note of interest is that polished rice is always present at both dinner and supper, mixed with other foods. The way rice is cooked makes it devoid of its natural vitamin B_1 content; the water in which it is boiled is discarded. This explains the modern trend of enriching all Cuban rice.

To demonstrate the significance of a conscientious study of nutrition in laborers, I mention the following personal experiences in our refinery.

Case 1. J. H., of the Painting Department, has been working for 30 years for the company, and has been a "problem employee" for the last 10 years. His habitual absenteeism and weary disposition for work make him an inefficient employee. His sickness disabilities have all the characteristics of chronic absenteeism: frequency, one day or two of duration, caused by subjective symptoms such as cephalea, abdominal pains, lumbosacral pains, etc. He has never come to the Medical Department for a physical examination.

He called on us for our opinion on infant feeding, having just had his first grandson. After a long and friendly conversation, he agreed, first, that the child would be seen by a competent pediatrician, and second, an appointment with him for a physical examination in our Medical Department. This revealed a white, 45 year old married man who had two sons. Under environmental history he related having started work-

ing when he was still a small boy as a fruit peddler. Had entered the employ of the company at 16 years.

His *chief complaints* were: poor appetite, asthenia, a tired feeling, more intense in the morning than at the end of his working day. He acknowledged that, although, not really sick, this asthenia was the cause of his frequent absences, and that he had to make up pains to keep his fellow workers from cataloguing him as indolent and lazy. He showed very little or no interest in his work or in getting ahead. His only interest was his new grandson.

His past medical history was without importance except for typhoid fever some 20 years back. His wife has had tuberculosis.

An inquiry into his eating habits showed poor appetite and most inadequate deficient meals,—breakfast—black coffee; lunch and supper—rice, viandas and meat on rare occasions. He complained that milk and eggs made him sick, but could not specify the symptoms as he had not eaten these foods for years. He used to drink alcohol liberally.

The *physical examination* revealed an undernourished man who looked older than his age. His weight was 103 lbs., height 65 inches, B.P. 120/80, P. 82. The skin was scaly and wrinkled, mucous membrane was pale, the tougue showed congested and hypotrophic papillae around the edges, and there was oral sepsis. The abdomen was soft and nontender; pulmonary auscultation and x-ray film of the chest were normal. *Laboratory investigations* showed: a trace of albumin in the urine; a hypochromic anemia of 4,800,000 RBC, a Hgb. of 72%, a WBC of 6,100 with a normal differential count, and a normal sedimentation rate.

We recommended intensive treatment with vitamins and minerals in addition to a balanced diet. At his request I visited his home to meet his grandson, and during this visit I interested his wife in cooking well balanced meals, especially improving her husband's breakfast. We advised him to come to our Medical Department every 15 days for a period of time.

After 2 years his weight rose to 132 lbs., the tongue lesions disappeared, he had his teeth repaired, and his appearance has improved in general. He has not been absent for more than a year. Even his home looks different because he has taken interest in improving his living conditions. The reports of his supervisors are very favorable.

Case 2. T. R., a 55 year old driver, has been in our company for 24 years. He works in a Depot of the Interior of the Island and came to our Medical Department soliciting a transfer from truck driving to another job because of difficulties of vision at night driving.

In this case we looked for and found, through a detailed dietetic inquiry, great lack of vitamin A intake. The eye specialist diagnosed hypermetropic astigmatism which would be relieved with corrective glasses. His final conclusion was that his visual disturbances were caused by vitamin A deficiency. Large doses of vitamin A were prescribed along with a diet rich in this vitamin. A year and a half later, the man is still working as a truck driver and all symptoms have disappeared.

Comment. These 2 cases have demonstrated the important part nutrition has played in their rehabilitation through the study of the patient's nutritional status. However, the cases of undernutrition will not always be so obvious. In most instances one detects a number of symptoms that may seem unimportant, such as atrophy, scaling and pigmentation of the skin, neuritis, anorexia, stomatitis, glossitis, cheilosis, angular stomatitis, diarrhea, hypochromic anemia, or easy of bruising.

Until now I have made reference only to the refinery workers. Among the office clerks at the Marketing Department, in Havana City, the nutritional problems are the reverse of those found in the workmen. Obesity and its complications occupy the first place as a consequence of the social level of these people and their sedentary jobs.

Preventive Measures

Industries located away from populous centers should have their own restaurants or cafeterias where workers may find appropriate food at reasonable prices. The industry medical department, with the aid of a dietitian, should supervise the planning of the menus which should be in accordance with the environmental eating habits.

To induce laborers into selecting adequate food, posters indicating balanced diets should be placed at the cafeterias entrance and other visible places. Some industries have gone so far as to reimburse the employee part of the cost of his food with the purpose of stimulating him into selecting good foods.

Sometimes these out-of-town industries will be surrounded by the houses of workers and their families in which case management may resort to commissaries. Other industries supply their workers with vitamins, but there is danger of the employee becoming negligent of balanced diets, thinking vitamins are enough to make up for deficiencies.

We have observed that the majority of our refinery laborers eat at home, since most of them live in two nearby towns, and that their nutritional problems come from bad selection of food. That is why the nutritional program must not stop at the working center, it must reach the home where his food is prepared.

As one considers any worker's home, it will be seen that it involves three different parts: the laborer, who spends most of the day at work; the child who goes to school every day; and the wife who takes care of the home and is in charge of the selection and preparation of the meals. It is obvious that this third party receives all the information given to the child in the school and in the working center to the laborer. Government should encourage nutritional programs in the schools, having all teachers stress the benefits of good nutrition. We should also take advantage of the press, radio and television as conveyors of information on nutrition through their programs to the public.

And lastly and more important to the physician in industry is the personal instruction to the employee on the occasion of his periodic physical examination.

Posters should be placed periodically in all visible places at the plant; they should be objective, interesting and humorous. A few of these have been done by our own workers. We also use the company's monthly publications for nutrition instruction and now and then publish pamphlets on nutrition counseling. Our aim is to create in the minds of the employees a conscience of good nutrition, just as the Safety Committee creates a conscience of safety.

Resume

The study of the nutritional status of the worker is of primary importance and a matter of great responsibility for the industrial physician as well as for management. Industrial medicine, that is, preventive and constructive medicine, will not be successful and productive if the nutritional status of the employee is not discovered and his deficiencies or excesses controlled and prevented.

A Critical Review of the Evolution and Treatment of Medial Fractures of the Femoral Neck*

ALBERTO INCLÁN COSTA, M.D., *Havana, Cuba*

The author describes his management of medial fractures of the femoral neck.

WE HAVE SELECTED A SUBJECT, well known to every one in this audience, and which has been discussed so frequently that scarcely anything more can be said which is of any importance. However, 42 years of orthopedic practice has permitted me to take a great part in Cuba in the evolution of treatment for this traumatic condition. This fact and a continuing attempt to find a better solution to the problem of treatment, provide sufficient excuse to try again to express my opinion on this subject.

When I started the practice of orthopedic surgery in Havana in 1916, after having spent two years at the Ruptured and Crippled Hospital under Dr. Royal Whitman and also at the Post-Graduate Hospital under Dr. Fred H. Albee, I found the treatment of fractures in the hands of the general surgeon who often left the fracture to be treated by an orderly.

Fractures of the neck of the femur were treated by continuous traction, according to the methods of Tillaux and Hennequin.[1] The results in medial fractures were so poor that for most patients, particularly the aged, it meant either death or permanent disability. Union, in this type of fracture, was seldom obtained. Pseudoarthrosis was the most frequent late complication with a high mortality due to the prolonged recumbent position and the development of pneumonia, intestinal paralysis, infected pressure ulcerations, or pyonephrosis which were common.

I introduced Whitman's abduction treatment for fresh fractures, the use of bone grafts for delayed and nonunion, and the hip reconstruction operations of Whitman, Brakett and Albee for nonunion with neck resorption and necrotic head. Later we started to use Leadbetter's treatment instead of Whitman's abduction, and the results improved considerably (50%) because we were able to mobilize our patients much more quickly and easily, and could let them stand and even walk with their casts.

It was quite difficult for me to convince our medical practitioners of the idea of employing surgical measures for treating fractures of the neck of the femur, by using the Smith-Petersen nail. As many other surgeons have done, we developed a guide to place the nail, thus avoiding open reduction of the fracture. X-ray control with anteroposterior and lateral views of the fracture was also done.

Absorption of the neck and aseptic necrosis of the head of the femur were frequent hazards in the postoperative evolution of cases treated by nailing, and we became aware of the fact that mechanical fixation alone, even with proper reduction of the fracture, was not sufficient to obtain the best results in these fractures.

Use of the Smith-Petersen Nail

In 1937, I presented at the meeting of the American Orthopedic Association, the first 4 cases in which I had used the Smith-Petersen nail as a mechanical fixation and an autogenous bone graft, following Albee's technic, to fill the biologic need in trying to restore the circulation of the ischemic head, and also as an active osteogenetic element at the fracture line. The reports of the results obtained with this method of treatment have been published. Union was obtained in 90% of the cases and aseptic necrosis of the head

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was reduced to 6 per cent. We have been satisfied with the results of this treatment, provided we can follow strictly the proper technic to avoid failures.

The operative risk should be evaluated by the internist and with previous laboratory examinations.

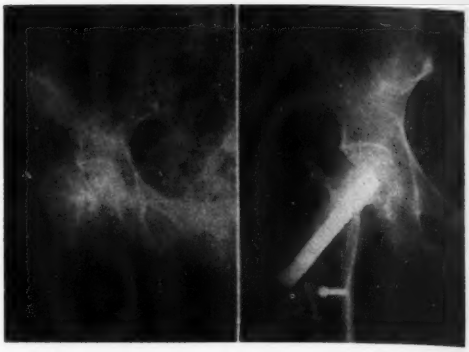
1. Subcapital and transcervical fractures of the neck of the femur should be reduced accurately and the reduction checked in two planes by x-ray films. Reduction should be obtained gently, avoiding excessive manipulation. Generally, we try to get an immediate reduction of the fracture, using continuous Buck extension and adding an upward pull to control external rotation. In many cases we are able to maintain this reduction on the orthopedic table without the need of other manipulation. In cases with impacted fracture and varus rotation of the head, Leadbetter's technic with lateral pull added, to modify the impaction, is used as gently as possible.

FIG. 1

A B C D

(Case 2) (A) A 72 year old woman. Subcapital fracture Powel 3. (B) Reduction and fixation with two Steinman pins. (C) Anteroposterior view one year after surgical treatment with Smith-Petersen nail and autogenous graft. No limp nor cane. (D) Lateral view of the hip after treatment.

FIG. 2



A B

(Case 2) (A) A 91 year old woman. Subcapital fracture Powel 3. (B) View after nail fixation and autogenous bone graft, showing union. One year after treatment walking without limp or cane.

2. We do not use general or spinal anesthesia. If reduction is necessary we use 20 cc. of a 2% Novocain intra-articularly. For the operation we use regional anesthesia with 0.5% procaine. If there is no special contraindication, epinephrine is added to the solution. The patient is prepared with sedatives and ganglionoplegic medication and a thorough double preparation of the operative field.

3. Radiographic control is done with two portable x-ray machines. The one used for the lateral view is kept in the same place after we have obtained a satisfactory view of the neck and head of the femur.

In many of our cases we have obtained the graft from the opposite tibia, under regional anesthesia, 7 or 10 days before; the graft, after having been properly shaped with Albee's bone-mill, is kept in our bone bank. We pay much attention to obtaining a perfect adjustment of the graft to the diameter of the tunnel made with the graduated drill which, at the same time, gives us the proper length of the graft.

4. The reduction obtained must be preserved without being disturbed by the insertion of the nail or graft. This is sometimes very difficult. If the fragments are displaced we start all over again. For many years I have been using two thick Kirschner wires, slightly converging toward the head, to avoid rotation

when the nail hits the condensed bone trabeculae of the head. These wires are also used as "guides" for directing the nail and the drill.

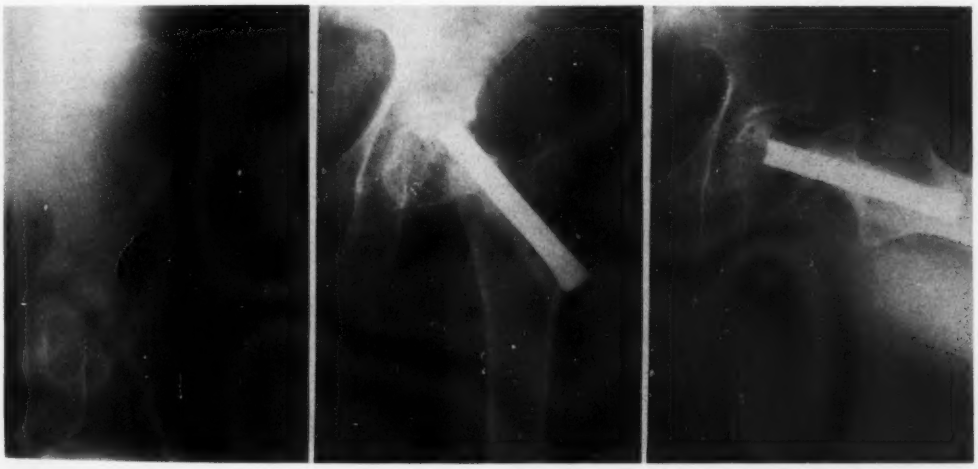
5. We have been placing the nail close to the border of the calcar femoris. We do not use cannulated nails of the Sven-Johansen type. It is important to cut the cortex with the nail starter to avoid fracture of the bone, which in older patients has become quite brittle. We have had this complication occasionally when we have tried to insert the nail directly. The nail should be started and another x-ray film made. If the direction is correct and a nail of proper length has been selected, we can continue its insertion. The latter should contact three points,—namely, the head, arch of the neck, and the femoral cortex.

6. We drill a tunnel parallel to the nail and the graft is inserted "like a cork in a bottle." This is a principle of bone grafting, forgotten by some orthopedic surgeons. Perfect adjustment of the graft to the recipient bone is indispensable for rapid revascularization of the graft. Square grafts do not fit in a round tunnel. The diameter of the perforation and graft should permit perfect contact of their respective surfaces.

7. Before suturing, more roentgenograms are taken for control of the position and the length of the nail and the graft. The patient is then placed on an orthopedic bed with enough traction to avoid muscular contraction. The limb is maintained in extension, 20 degrees of abduction and slight internal rotation. This position must be carefully watched by both the surgeon and the nurses. Daily passive motion of the hip in flexion, abduction and internal rotation, and also flexion of the knee should be done by the surgeon or his assistants.

After 2 weeks when the wound is healed, traction is removed and a light plaster cast is substituted up to the knee with a check bar to avoid external rotation. Then the patient may be moved to a wheel chair, maintaining the limb in the same position. Any pain or limitation of internal rotation urgently demands another x-ray examination of the hip. Semi-active motion, accompanying the passive one, carried out by the surgeon is possible during the following weeks. Active motion without weight bearing is allowed during the last 4 to 6 weeks before standing, or walking with crutches or cane is permitted. *Only when x-ray evidence of union, with bone trabeculae crossing through the fracture line,* is present should the patient be allowed to bear weight. Physiotherapy will be necessary for 8 to 12 weeks according to the amount of cooperation given by the patient.

FIG. 3



A B C

(Case 3) (A) A 62 year old woman. Late subcapital ununited fracture with absorption of the neck and coxa vara treated in 1935. (B) Two years after operation. Follow-up 22 years. Complete restoration of function without need of cane for walking. Nail placed on top of the graft. (In our present technic we prefer placing the nail underneath, in contact with calcar femoralis) (C) Lateral view at the same date.

Perhaps I have been too meticulous in the description of our routine technic for the treatment of this controversial fracture, but to maintain our point of view, I needed to emphasize the necessity of complete adherence to each and every one of the details enumerated, before one can blame the method for a failure. I believe this method of treatment will greatly reduce the aseptic necrosis of the head of the femur, and the number of cases of nonunion which follow the use of nails, screws, bolts, wires and other mechanical means of fixation of this fracture. I will try to prove this statement with the presentation of a number of cases which will demonstrate the value of the bone graft, as an osteogenetic factor, and also its participation in restoring the circulation of the head.

Review of the Recent Literature

A review of the literature in the last few years, adds more controversial points in relation to the treatment of this fracture. On the one hand: the efforts to ascertain the viability of the head by the use of radioactive phosphorus published by Boyd;[2] the new studies of the blood supply of the head of the femur in adults, reported by Trueta and Harrison;[3] the experimental study of the rate of revascularization in autogenous, homologous and heterologous grafts, published by Stringa;[4] and the recent report on the time of appearance of aseptic necrosis in femoral heads after fracture, made possible by the resection of the head of the femur in recent and old fractures at the time of a substitution operation for implantation of an internal prosthesis as presented by Coleman and Compere[5] at the last meeting of the American Orthopedic Association, are of great interest to every orthopedic surgeon. The fact that of 25 femoral heads removed during the first three weeks following fracture, none showed complete necrosis, and that in those studied at four or five days following fracture active osteogenesis was noted, are particularly interesting to every one dealing with a possible preservation of the femoral head in these fractures. These reports increase our belief that a bone-graft properly placed can be revascularized in time to avoid early necrosis of the head of the femur, if it is done during the first few days after the fracture.

FIG. 4

(Case 6) 12 year old boy. Transcervical fracture of the neck of the femur.

On the other hand, since Robert and Jean Judet[6,7] reported (1946) their experience with the use of an acrilic prosthesis as a substitute for the femoral head, the idea of applying this "resection reconstruction operation" to recent fractures of the neck of the femur has added important controversial points, which have further complicated the selection of the proper surgical measure to eliminate the hazards of the end results in the treatment of this type of fracture.

In my community as in many others, statements like this have been made: "All medial fractures of the neck of the femur in patients of 60 years of age or more should be treated by excision of the head and replacement with an internal prosthesis."

After treating this fracture by different methods, each new one showing improvement in our results, I consider such a statement extremely radical, in spite of the fact that it is subscribed to by such prominent surgeons as the Judet brothers, Mc. Ausland,[8] O'Brien, Day and Hinchey[9] and others.

Thompson,[10] creator of one of the most

commonly used metallic intramedullary prostheses, considers this treatment a "salvage method," and not a routine procedure in fresh fractures in older persons. In one of his publications he states, "A well healed and well nailed fracture of the femoral head, that has not developed circulation changes is better than any type of hip prosthesis. Such a femoral head is alive, and with normal metabolism it should serve the individual until his death." He considers the early use of the prosthesis contraindicated in fresh fractures except in rare instances, as in, fractures occurring in an aseptic necrotic head, in radium necrosis fracture of the femoral head, in tumorous conditions of the head and neck, and in shock therapy fractures in mental cases.

Cleveland and Fielding,[11] after a criticism on the tendencies "to advocate the immediate use of a metal or plastic substitute for the femoral head in fresh fractures of the neck of the femur," concludes, "There is no really satisfactory substitute for an intact femoral head and neck." They only accept the use of an internal prosthesis as a "salvage method" in cases of nonunion of the fracture or circulatory disturbance of the femoral head.

None of the above mentioned orthopedic surgeons have considered the use of a bone graft and nail as primary treatment of the fracture.

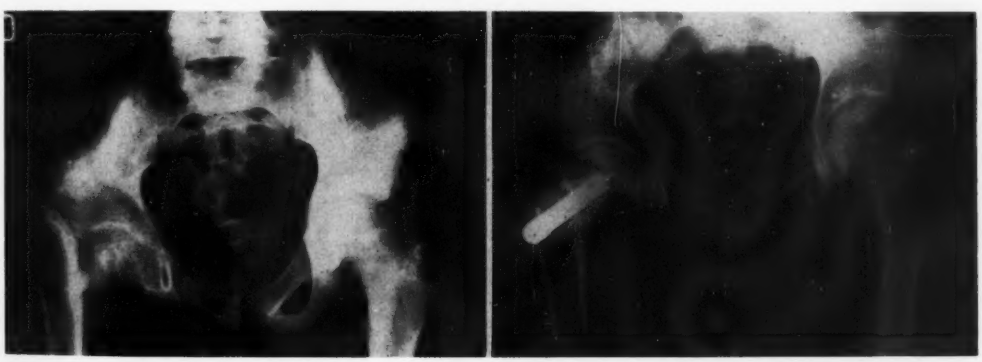
I have used an internal prosthesis in a number of cases in which there was great absorption of the neck and a necrotic head as a salvage reconstructive procedure, being aware of the uncertainties of the end results, because of the possibilities of different types of complications, sometimes in the immediate postoperative period, and sometimes as late disturbances produced by the use of the prosthesis.

Mendelsohn and Becker[12] have reported their experience in 100 cases of replacement arthroplasties of the hips, with honest evaluation of the complications observed. Early postoperative complications, within the first two months after operation were as high as 50%; pain, infection and dislocation were the most frequent complications. In 40% of the cases some late complications developed, para capsular calcification and central and superior migration of the prosthesis were the most common. The authors remarked, "The insertion of a hip prosthesis is not a minor procedure."

I must add that in the cases in which I have been obliged to remove an internal prosthesis, the rehabilitation of the hip joint for weight bearing has been a difficult problem to solve.

However, it is encouraging to find in the literature of the present year, a number of articles demonstrating the constant desire of authors to develop new methods of treatment of the "unsolved fracture," searching for its definite and permanent solution. Before closing I would like to comment briefly on three of these contributions.

FIG. 5



A B

(Case 6) (A) Ten months after fracture, treated by traction for 50 days and weight bearing before union was obtained. X-ray shows almost complete absorption of the neck and upward displacement of the trochanter with nonunion. (B) One year after nailing and double bone grafts. Shortening of the neck and coxa vara. Excellent functional result. (The result in all of these cases demonstrated in moving pictures.)

Ottolenghi[13] has developed a new technic for nail fixation of this fracture. This "biomechanical" method is based on the best control of the three fundamental factors of displacement of the fragments in fractures of the femoral neck, enunciated by Habousch.[14] These factors are,—moment of flexion, moment of rotation and axial pressure. In order to control the first factor he places a long biflanged nail in contact with the calcar femoralis, the center of the head and the external cortex of the femur. By doing this the lever branch of the nail is shortened, allowing greater pressure without tendency to flexion dislocation of the head. The moment of torsion is controlled by the use of a short plate at the end of the nail that will fix it to the lateral aspect of the femoral diaphysis, using two screws to hold it in place. The almost vertical position of the nail close to the weight bearing line, allows a better support of axial pressure. No end results have been published yet.

Another interesting paper by Charnley, Blockey and Purser,[15] describes the principles of interpressure of the fragments to obtain union. For this purpose they have developed a new lag screw and, through the use of a spring, a pressure of up to 25 pounds can be maintained at the fracture line. The screw is fixed with a plate to the external aspect of the femur by five screws. The authors claim that the insertion of this ingenious device is easier than the insertion of the Smith-Petersen nail. Also, that the spring action draws the fragments together, even when absorption is present, and gives constant account of any vascular complication. The mechanism is different from that of the nail designed by Schumplelick and Janzen and by Pugh. Results have improved 30% over those which have been obtained with the Smith-Petersen nail.

The last paper I wish to comment upon is by Godoy Moreira[16,17] and de Camazo. After 17 years of exhaustive work trying to solve the treatment of medial fractures of the neck of the femur, using first a lag screw of his own design and other methods of mechanical fixation, he has finally arrived at the conclusion that the physiologic problem of this fracture must be solved. They have added to the use of the screw a tibial graft parallel to it; through a second incision he opens the joint and packs the line of fracture with cancellous bone, through an opening in the wall of the neck. They emphasize in this paper that "every fracture of the neck of the femur must be treated from the start as a pseudoarthrosis."

As you can see, we are still "on the march" toward our goal,—a definite and successful treatment of the medial fractures of the neck of the femur. Let us persist in our aim and not fall into a defeatist attitude. As orthopedic surgeons we must try to cure the fracture, and leave the use of artificial substitution as a salvage procedure when we are convinced that there is no other choice. We sincerely believe a perfect alignment of the fragments before, during and after an absolute internal fixation, plus an autogenous bone graft to aid osteogenesis and revascularization of the head, is the best we can actually offer for medial fractures of the neck of the femur.

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Epidermoid Cysts of the Testicle

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Admittedly it is safe policy to think in terms of orchiectomy when facing the management of a tumor of the testis. Rarely, as described in the cases reported herewith, clinical judgment may save an organ in a certain few instances of small tumors.

PURE EPIDERMOID CYSTS of the testicle are rare. It is the purpose of this report to add 3 cases to the 9 previously reported instances[1-7] and to discuss briefly their surgical management and pathology.

Case Reports

Case 1. W. F. (No. 56-6316), a 17 year old white boy, was admitted to Presbyterian Hospital on July 19, 1956. For 2 months the patient had noted a small firm mass in the right testicle. Other than this no subjective symptoms had been noted.

Physical examination was unremarkable except for the right testicular mass, which was firm, nontender, located in the anterior aspect of the gonad and definitely separate from the epididymis. Routine laboratory studies, including S.T.S., were not contributory. Chest x-ray film and gonadotropic studies yielded no further information.

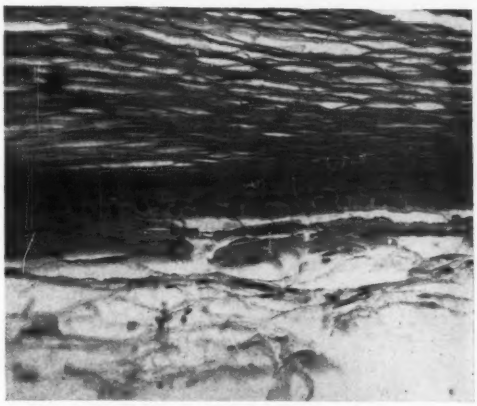
At operation a 1.2 cm. mass could be palpated just beneath the tunica albuginea. It was firm, oval and sharply demarcated from the surrounding normal testicle. A 2 cm. incision was made through the overlying tunica and the encapsulated cystic mass easily enucleated. Immediate frozen sections disclosed a benign lesion. The tunica and scrotum were closed, and recovery was uneventful.

The cyst contained merely laminated yellowish grumous material. The wall measured up to 1 mm. in thickness. Microscopically the lumen was filled with desquamated keratin material (Fig. 1). The surrounding wall was composed only of thin well differentiated keratinizing stratified squamous epithelium with an easily discernible granular layer. No cutaneous adnex or derivatives of other embryonal germ layers were present. A small rim of adjacent connective tissue was attended by a few remnants of atrophic seminiferous tubules. (The entire specimen was studied microscopically.)

Case 2. H. S. (No. 56-7615), a 37 year old diabetic truck driver, was admitted to Presbyterian Hospital on Sept. 4, 1956. Five months previously his internist noted a painless hard mass in the right testicle, but the patient refused investigation. Two weeks prior to admission to Presbyterian Hospital, he developed a paralysis of the left facial nerve, and his internist insisted that he consult a urologist. The patient had been aware of no change in the testicle and gave no history of trauma, tuberculosis, syphilis or chronic disease. He had had no pain or weight loss. He had been aware of a decrease in the degree of erections, but had no definite feminizing symptoms.

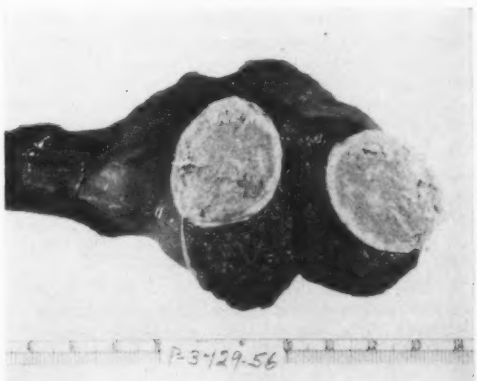
In the lower portion of the right testicle there was

FIG. 1



(Case 1) Wall of epidermoid cyst with keratin-filled lumen above. (H & E X 240.)

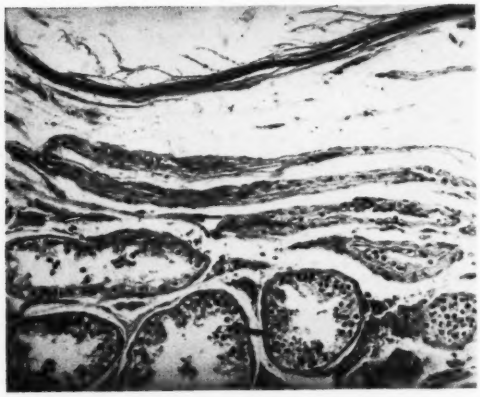
FIG. 2



(Case 2) Black and white reproduction from color photograph. Note discreetness of keratin-filled cyst.

†From the Departments of Urology and Pathology, Presbyterian Hospital, Charlotte, N. C.

FIG. 3



(Case 2) Note very thin squamous epithelium lining cyst in upper portion of field. (H & E X 120.)

a hard nontender mass which did not transilluminate. The upper pole was normal in consistency and the epididymis and vas deferens were not involved. Except for the facial weakness, the physical examination was otherwise normal. Routine laboratory studies, including the S.T.S., were normal. Preoperative chest films, I.V. pyelograms, and gonadotropins were normal.

The preoperative diagnosis was testicular malignancy, and an inguinal orchiectomy was carried out.

Beneath the tunica albuginea and in the midportion of the testis was a discreetly encapsulated, uninodular cyst filled with grayish laminated material (Fig. 2). It measured 3 by 2 by 2 cm. and could be shelled out easily. Microscopically it was filled with desquamated keratin, and lined with normal appearing keratinizing squamous epithelium situated upon a thin zone of hyaline connective tissue (Fig. 3). The contiguous parenchyma of the testis was concentrically compressed. Numerous histologic sections disclosed no structures resembling cutaneous adnexa nor derivatives of other embryonal germ layers. The epididymis and spermatic cord were normal.

Case 3.* O. C. (No. 101370), a 36 year old white man, was admitted to Charlotte Memorial Hospital in May, 1950. During the course of routine physical examination shortly prior to admission, a mass was noted in the right testis. There had been no tenderness or other subjective symptoms, and the mass had not been noted by the patient.

At operation a yellowish white mass was seen in the midportion of the testicle beneath the tunica albuginea. The surrounding testicular tissue appeared normal. An orchiectomy was done, recovery was uneventful, and on examination 4 years later there was no evidence of any recurrence or metastasis.

Grossly the mass consisted of a cyst 1.6 cm. in diameter, containing a pale bluish laminated material in its lumen. The cyst wall was lined with extremely thin keratinizing stratified squamous epithelium, adjacent to which was fibrous and hyalinized connective tissue (Fig. 4). Multiple sections disclosed no skin appendages, or derivatives of other embryonal germ layers.

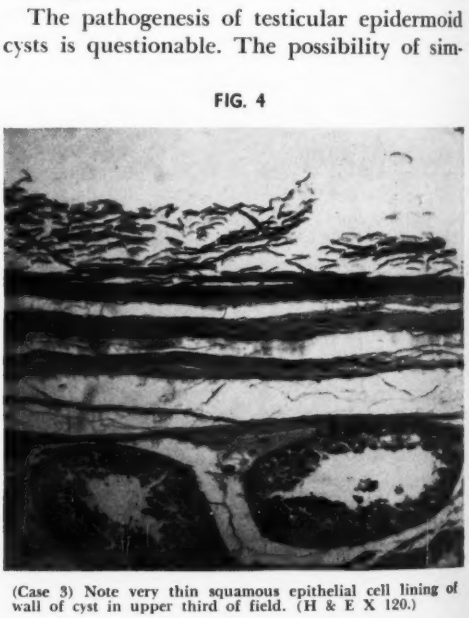
*We are grateful to Dr. Robert W. McKay and Dr. Paul Kimmelsteil for making this case available.

Discussion

Several extensive reviews of testis tumors do not mention epidermoid cysts.[8-14] Dockerty and Priestly[1] reported the first case, which occurred in a 35 year old white man. Table 1 illustrates the pertinent features of the 12 reported cases, including our own. Without drawing conclusions from a statistically inadequate series, it is of interest that all have been adults (youngest 17 years), and that the 9 about whom race was mentioned have been white. The majority of tumors have been asymptomatic painless lumps or enlargements, therefore only accidentally discovered by the patient, or in some instances discovered incident to a physical examination. Most have been 2 cm. or less in size, and described as solitary nodules or unilocular structures. The larger ones seemingly produce a diffuse testicular enlargement. When examined pathologically, all have been keratin-filled solitary oval or spheric cyst with discreetly delimited walls capable of being "shelled out" from the surrounding tissue. Cases with cutaneous appendicular structures or various elements encountered in multidermal teratoid tumors have been excluded from consideration in this report.

The pathogenesis of testicular epidermoid cysts is questionable. The possibility of sim-

FIG. 4



(Case 3) Note very thin squamous epithelial cell lining of wall of cyst in upper third of field. (H & E X 120.)

TABLE 1

Author	*Year*	*Age*	*Race*	*Testis*	*Known Duration*	*Testis Enlarged*	*Tumor Size*	*Pain*	**Operation*
Dockerty and Priestly	1947	35	W	R	? gradual enlargement	Asymmetrical nodule	2.5 cm.	No	O
Gage and Brodie	1950	35	W	R	? incidentally discovered	50% larger than left	3 cm.	No	O
Mooslin and Schulte	1951	55	?	L	28 yrs.	Diffuse	4 by 5 cm.	Slight transient aching	O
	1951	21	?	L	3 das.	Central nodule	1 or 2 cm.	None?	O
Jensen	1952	26	W	R	7 mos.	Mass anterior testis	?	No	O
Cook and Kimbrough	1954	29	W	L	5 yrs.	Solitary nodule lower pole	1.2 cm.	Tenderness	SE
	1954	24	W	R	Incidentally discovered	Solitary nodule superior pole	1.2 cm.	No	SE
Nagel and Polley	1955	37	W	L	4 mos.	Round unilocular	2 cm.	No	O
Olsen and Calderin	1955	22	?	R	2 wks.	Solitary nodule	1.5 cm.	Yes	SE
Authors' cases	1956	17	W	R	2 mos.	Solitary nodule	1.2 cm.	No	SE
	1956	37	W	R	5 mos.	Solitary nodule	3.0 cm.	No	O
	1956	36	W	R	Few das.	Solitary nodule	1.6 cm.	No	O

*O: Orchiectomy
SE: Simple excision of cyst

ple metaplasia of seminiferous tubular epithelium, possibly related to inflammation in the genitourinary tract, has been suggested.[7] Nagel and Polley[6] have recently stressed the possible teratoid nature of the lesion, whereby entodermal derivatives become obliterated secondary to the expansion of the cyst. They presented an excellent review of the diverse teratologic theories which need not be restated here. The interested reader is referred to their excellent discussion. We are inclined to agree that available evidence suggests that the testicular epidermoid cyst is probably a completely differentiated, therefore adult and utterly benign teratoid lesion. It may have had its inception as a unidermal (ectodermal) growth, however, since there is no evidence of derivatives of other germ layers. The absence of inflammation or other lesions with which metaplastic phenomena are known to be associated elsewhere in the body fails to support the theory of seminiferous epithelial metaplasia. Moreover, direct squamous metaplasia of seminal tubular elements has not been observed to our knowledge.

Recognition of the benign nature of the lesion may justify simple excision. A larger cyst embedded within the testis such as one measuring 4 by 5 cm. encountered by Mooslin and Schulte,[3] would have produced such retrogressive or atrophic changes that preservation of the gonad becomes irrelevant. The same is true of the second case reported in this series. Organ function may not be significantly impaired with the smaller cysts, and their simple excision can be accomplished with safety and preservation of the organ. We suggest that the occurrence of a single asymptomatic unilobular nonhemorrhagic small testicular mass might be surgically explored. If not encapsulated, or sharply defined, orchiectomy is imperative, but otherwise immediate consultation and frozen section by the pathologist may indicate the prudence of local excision. It is our impression that many, if not the majority, of urologists and surgeons, recognizing the malignant potentialities of the vast majority of testis tumors, reject any procedure less than orchiectomy for any testicular tumor or potential tumor. In fact it has been said, "opening the tunica albuginea . . . for diagnostic purposes is in general not to be recommended. If this is necessary, it is felt by most genitourinary surgeons, an orchiectomy should be performed and any further exploration done by the patholo-

gist. . . ."[15] To this we subscribe heartily for the great majority of testicular tumors, but exploration of the small solitary asymptomatic nonhemorrhagic tumor would seem to be justified by the occasional, or infrequent benign lesion not requiring ablation of the gonad.

Summary

Three cases of benign epidermoid cysts of the testis are reported. This brings the total to 12 of such lesions described.

All cases have been reviewed and certain salient features tabulated. Mention is made of the pathogenetic theories. We favor the teratoid hypothesis.

The possibility of safe conservative treatment is exemplified in one of our cases, and in 3 from the literature.[5,7] The relative size of the lesion in our second case made preservation of the testis irrelevant. In case 3 the lesion was not recognized due to the fact that the testicle was enucleated with a portion of the cord through an inguinal incision without inspection of the testicle.

Encapsulation, uninodularity, and absence of pain, hemorrhage, or necrosis are the criteria which indicate the feasibility of considering conservative management. If local excision of the tumor is done, close cooperation and consultation between the operator and the pathologist is necessary at the time of exploration. Finally, it should be emphasized that the wall of the cyst should be completely examined by the pathologist in order to assure that no other dermal derivatives exist. If other derivatives should be found, the scrotum can be reopened for complete extirpation of the testis, epididymis, and adjacent spermatic cord.

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Management of Common Problems in the Urinary Tract of Children*

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A number of anomalies may occur in the genitourinary tract. Their early diagnosis and proper management may prevent irreversible damage which may shorten life in later years.

MOST OF THE COMMON PROBLEMS referable to the urinary tract in children are due to some type of congenital anomaly. The incidence of urinary complications of many acquired lesions has been reduced through expansion of pediatric knowledge and developments in preventive medicine.[1]

Failure to follow the normal developmental pattern results in a higher incidence of congenital anomalies in the urinary tract than in any other system. Because of their intimate embryologic origin, anomalies in the genital and urinary tracts are commonly associated.[2] The degree of maldevelopment varies from one individual to another and a basic knowledge of embryology is required for reasonably accurate evaluation.

The cases fall largely into two groups: (1) children with external defects that are immediately apparent, and (2) those with internal deformities that are not readily recognized. The latter group is comprised chiefly of obstructive lesions. The fact that these lesions are the result of defective development and are prone to produce progressive damage to renal function emphasizes the importance of their early recognition. Symptoms that lead to early recognition are not always helpful. They range from abnormalities in the voiding pattern to signs of renal failure.

Two years ago we reported results of a study of 129 children younger than 10 years of age with obstruction in the lower urinary tract.[3] Since then 45 additional children have been treated; this brings the total number to 174 patients treated surgically on our service for urinary obstruction during the past 13 years. The symptoms presented by this group included frequency and straining to urinate, urgency, overflow incontinence, acute retention, signs of renal failure, hematuria, either gross or microscopic, and enuresis.

Symptomatology of Obstructive Lesions

Enuresis is the most common urinary disturbance in children. It is functional in most cases and urologic investigation on the basis of enuresis alone is usually not carried out on children less than four years of age. The majority of these children have urinary control by that time. Of the children examined by our staff because of enuresis alone, approximately 28% had some degree of obstruction in the lower urinary tract producing vesical irritability. A diurnal type of enuresis is of more significance and rarely occurs in the absence of urologic disease.

Straining to urinate is perhaps the earliest sign of obstruction of the lower urinary tract and the one most frequently overlooked. This should be observed during infancy. The incidence of acute retention in children is low. It occurred in only 6 of the 174 cases reviewed. In other cases hematuria led to investigation of the urinary tract. It was gross in 8 cases and microscopic in others. In the majority of these infection was present, and in some hematuria was initiated by injury chiefly in those children old enough to indulge in some type of sport. A recent example is that of a 16 year old boy who sustained an injury to the right flank during football practice. He had never complained of any previous urinary symptoms. In the course of investigation of the extent of the injury, infection and microscopic hematuria were found. Complete urologic studies showed obstruction of the bladder neck, and associated obstruction at the right ureterovesical junction, and congenital absence of the left

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kidney. Other children showed signs of renal failure and one had hypertension which resulted from unilateral atrophic pyelonephritis. In one patient the condition progressed to the stage of bilateral hydronephrotic atrophy of the renal cortex without apparent urinary symptoms. This wide variation of symptoms, some of which may appear insignificant, emphasizes the importance of careful investigation of the voiding pattern in children and of attaching the same significance to variations from the normal that are accorded to dietary disturbances.

It would be superfluous to review the various types of obstructive lesions that are encountered. These have been adequately reported in the literature from the various centers where a large number of children are seen, and are available for review. It should be remembered, however, that congenital lesions are often multiple and one's attention should not be concentrated on one lesion at the expense of overlooking another of perhaps equal importance.

Stenosis of the external urethral orifice is a common finding that is encountered with about equal frequency in both males and females. Its clinical importance is equal to that of any other obstructive lesion and it may produce irreversible renal changes. Associated obstructive lesions in the upper part of the urinary tract, as well as other developmental defects, are frequently encountered. The fact that these defects are commonly encountered in association with developmental anomalies in the genital tract emphasizes the importance of study of the urinary tract in the management of such genital abnormalities as hypospadias and undescended testes.

Diagnosis

The diagnostic studies are well established and easily accomplished. These include the routine renal function tests and chemical and bacteriologic studies of the urine. The excretory urogram affords an estimate of renal function and may indicate variation from the normal as well as other developmental anomalies. Retrograde cystography is the most valuable of the urographic studies. It will indicate the size and architecture of the bladder, and will show the presence or absence of vesicoureteral reflux. In children old enough to cooperate a voiding cystogram will supply more information concerning the type and location of the lesion. Recent studies suggest that congenital prostatic valves are more common than was formerly believed and are more adequately demonstrated in the voiding cystogram.[4] An endoscopic examination will complete the urologic study and should be done with use of an anesthetic for reasons of accuracy. The diagnostic studies must be accurate and their results critically evaluated in order to distinguish those which require surgical treatment from those in which it would be contraindicated. Retrograde pyeloureterograms rarely contribute useful information and only increase the radiation exposure.

The ease with which urographic examinations can be carried out in children has made possible the management of many problems referable to the urinary tract that would otherwise not be recognized. On the other hand, the hazards associated with these studies have apparently not been sufficiently emphasized. The genetic effects of roentgen rays during diagnostic procedures should be familiar to the radiologist and urologist alike. The urogram is the most dangerous from the standpoint of gonadal injury. The testes are more vulnerable than the ovaries because of their more superficial location. There is no minimal threshold below which there is no damage, and once damage occurs it is irreparable. The maximum gonadal dose allowable during the first 30 years of life has been variously estimated to be from 14 to 30 roentgens. It has been established that mutations occur from genetic damage. It should be required that gonads be protected in children and adults up to the age of 35 years. It is the responsibility of the urologist to determine the minimum number of diagnostic exposures required in each examination and to see that gonadal protective mechanisms are provided.

Treatment

A detailed discussion of the operative treatment of obstructive lesions of the lower urinary tract is not indicated. There are individual preferences as to the method of approach and good results can be obtained from each method provided all obstructive tissue is removed.

The most troublesome complication of obstruction of the lower urinary tract is vesico-

ureteral reflux. The current controversy concerning its significance and its management is widely known. A few comments, however, seem appropriate. First of all an attempt should be made to differentiate the ureter dilated as a result of obstruction from the one that is due to neuromuscular maldevelopment. From the standpoint of those that are the result of obstruction, an attempt has been made to evaluate the various methods of management after the obstructive lesion had been removed. We first tried continuous drainage, either by an indwelling urethral catheter in females or suprapubic cystostomy in males, and have seen the condition progress as a result of infection and bladder spasm. We next tried the variously recommended plastic operations on the ureterovesical junction with considerably less than satisfactory results and for the present have discontinued their use. These patients are currently put on a voiding schedule that permits maintaining sterile urine and, in the majority of cases, this appears to prevent further dilatation if strict adherence to the schedule is observed. This requires education of the child and cooperation of the parents.

At the same time that emphasis is being placed upon the importance of signs that lead to the early recognition of the obstructive lesions, equal attention should be directed to the large group of children with symptoms referred to the urinary tract but without any lesion that requires surgical treatment. Urinary infection is a common complication of obstruction. On the other hand, it is encountered frequently in children without obstruction. It is a common complication of infections of the upper respiratory tract especially recurrent tonsillitis, and also of nonspecific vaginitis in females. From the numerous articles that have appeared in the literature during the past few years, it is apparent that both urologists and pediatricians have become overconscious of the surgical lesions that occur in the urinary tract in children at the expense of those that should not be operated upon. Therein lies the necessity of a critical evaluation of the results of diagnostic studies.

Other Anomalies and Their Treatment

Duplication is the most common anomaly of the upper part of the urinary tract. In the majority of cases it is of no clinical importance. On the other hand, if the duplication is complete, an orifice may be located in an ectopic position. In the male the ectopic opening is usually proximal to the external sphincter and there are no symptoms until the hydronephrotic segment becomes infected. In the female, however, the ectopic orifice is nearly always distal to the external sphincter and there is constant dribbling of urine. The usual location is in some part of the distal urethra or vagina. The voiding pattern is always suggestive, and is usually distinctive enough to differentiate this group from those with total urinary incontinence. In addition to dribbling these patients void in normal amounts and at the normal interval. The ureter that opens in an ectopic position never functions normally and there is always some degree of hydronephrosis and reduced function of the corresponding renal segment. An ectopic orifice may be difficult to locate; it cannot always be catheterized and the function of the renal segment may be reduced to the extent that it will not show in the urogram. Most of these anomalies involve the upper pole of the kidney and duplication is suggested if there is an abnormal amount of renal tissue above the lower segment that shows no evidence of compression deformity.

Treatment of ureteral duplication obviously must be individualized. If the involved segment has normal function, a liberal anastomosis may be established between the two pelves and the ureter ligated adjacent to the anastomotic site, or the duplicated ureter may be severed and implanted into the bladder. There are recognized complications associated with each of these procedures and they should be used only if the renal segment is important to the total renal function. In the majority of cases the corresponding segment is small, and the practical solution is segmental resection of the kidney with removal of the ureter if it is severely dilated and infected. Uninfected ureters may be left alone.

Exstrophy of the bladder is a common developmental anomaly of the urinary tract. The clinical problem it presents has long been recognized but there is considerable diversity of opinion as to the operative procedures that should be utilized in its manage-

ment. They range from attempts to reconstruct the bladder and urethra to cutaneous diversion of the urinary stream. There is perhaps no case in urologic practice in which a basic understanding of embryologic development is of more importance to accurate evaluation than exstrophy of the bladder. It must be recognized that in a significant number of cases there is some degree of absence of the urogenital diaphragm which is important to the ability to obtain urinary continence from attempts to reconstruct the bladder and urethra. In our hands, this procedure has not been satisfactory and at least for the present we have discontinued its use.

An incompetent anal sphincter is a common part of the developmental anomaly in these cases. To determine the competency of the rectal sphincter is an essential part of the preliminary study of patients in whom diversion of the urinary stream to the rectosigmoid is contemplated. This has long been a popular procedure in many medical centers and is still widely used. The complications that follow anastomosis of the ureters to the intact bowel are well known. The frequency and severity of these complications have led to development of other means of management. For those patients who have an incompetent anal sphincter the only alternative is cutaneous diversion. Development of the ileal conduit and the results obtained from its use have led to its increasing application in the management of exstrophy of the bladder. This procedure offers an acceptable solution to the problem presented by patients with an incompetent rectal sphincter. It appears to be relatively free from electrolyte imbalance and the other well-known complications that lead to renal failure. It also offers a satisfactory solution in those cases in which complications referable to the upper urinary tract have followed ureterosigmoidal anastomosis. It will not at this time be generally conceded that ureterosigmoidal anastomosis should be abandoned in all cases in which it can be utilized. Many patients with ureterosigmoidal anastomosis have been observed for a period of years without showing any evidence of significant loss of renal function and these cases may be considered satisfactory. There are also other factors to be considered. As a part of the developmental anomaly there is stenosis of the ureteral orifices of sufficient degree to require early correction in many cases, usually in the first six months of life. In this age group it is difficult to fit a collecting bag to the stump of an ileal conduit. In patients with rectal continence in whom early operation is indicated, ureterosigmoidal anastomosis is a justifiable choice. This is especially true in the case of females whose social activity would be more handicapped by wearing a collecting apparatus. If renal complications develop, construction of an ileal loop can always be carried out and usually by this time the child is large enough so that a bag can be adequately fitted.

The bladder dysfunction that results from spina bifida constitutes one of the most difficult problems in urologic practice. Spina bifida, like all other developmental anomalies, will vary in degree from one individual to another according to the amount of damage or degeneration of the nerve roots. The nerve lesion is of the lower motor neuron type, and the urinary dysfunction falls roughly into two groups, that is, those with incontinence and those with retention. Patients with a severe degree of spina bifida have total urinary incontinence because of the deficient nerve supply to the sphincteric mechanism. Other patients with lesser defects may sustain the principal deficiency in the nerves to the detrusor muscle with the nerve supply to the external sphincter relatively intact. Such patients usually have some degree of urinary control, but because of the imbalance between the strength of the detrusor and the resistance offered by the bladder outlet, residual urine and characteristic obstructive changes gradually develop.

As in the other anomalies, the method of treatment used must be individualized to fit the pattern of the anomaly. For those patients with a flaccid bladder outlet the ileal conduit appears to be the most satisfactory procedure. From the group with the residual urine may be selected patients who can be subjected to transurethral resection with reasonable expectation that an acceptable result can be obtained. An attempt is made to weaken the bladder outlet enough to permit complete evacuation of the bladder contents and therefore permit a longer interval between voidings. The entire circumference of the bladder neck must be resected from the

internal vesical orifice to and including the proximal margin of the external sphincter. Obviously, the margin of safety between retention and incontinence in this procedure is rather narrow. An open procedure on the bladder neck, such as applied to non-neurogenic lesions, is not satisfactory for this type of case. Manual compression over the bladder area during the voiding act is usually necessary to accomplish complete emptying. If a satisfactory result is not obtained from transurethral resection, these patients should be treated in the same manner as those with a flaccid bladder outlet. In contemplating a plan of treatment for this group of cases we must recognize that no mechanical procedure is an adequate substitute for a normal nerve supply. Efforts should be directed toward corrective means that will permit these individuals to move in some degree of normal social and occupational environment.

Summary

Most of the common problems referable to the urinary tract in children are due to congenital anomalies. These may be classified into, (1) external defects, and (2) internal deformities which are primarily obstructive lesions.

The symptoms of obstructive lesions include enuresis, urinary frequency, straining, urgency, incontinence and acute retention, hematuria, and signs of renal failure. Diagnostic studies are easily accomplished. They include renal function tests, chemical and bacteriologic examination of the urine, and urography. Treatment of obstructive lesions of the urinary tract is surgical removal. There are individual preferences concerning the method of approach. If all obstructive tissue is removed, good results can be obtained by each of these methods.

Other developmental defects of the urinary tract encountered in children include duplication, exstrophy of the bladder and vesical dysfunction resulting from spina bifida. In most cases duplication is of no clinical importance. If the duplication is complete, an orifice may be located in an abnormal position and cause urinary symptoms. Treatment must be individualized.

Exstrophy of the bladder is a common developmental anomaly of the urinary tract. There is no unanimity concerning the surgical treatment to be employed. Operations for its correction range from attempts to reconstruct the bladder and urethra to cutaneous diversion of the urinary stream.

The bladder dysfunction caused by spina bifida constitutes one of the most difficult urologic problems. In contemplating a plan of treatment the urologist must realize that no mechanical procedure is an adequate substitute for a normal nerve supply. The aim in surgical correction should be to enable the patient to live in some degree of normal social and occupational environment.

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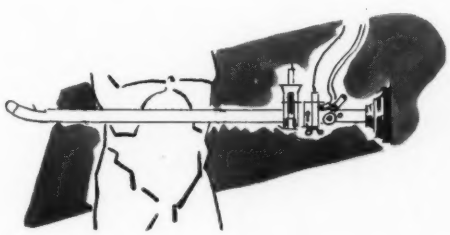

Prevention of the Radiation Hazard in Diagnostic Urology*

ROBERT LICH, JR., M.D., and
HOWARD D. BUMSTEAD, R.T.,† *Louisville, Ky.*

In 1955, Robbins and Hendricks[1] reported their results of measuring the radiation to which the urologist was exposed during retrograde urography. These authors introduced a simple solution to the problem of excessive exposure to radiation of the practicing urologist. It is the purpose of this paper to emphasize the importance of this study and advocate the universal adoption of their simple protective measure. In addition to substantiating the work of Robbins and Hendricks, we have extended their study to include measurements of the radiation penetration of the cystoscopic table and secondary floor scatter.

The protective measure to control scatter at the time of diagnostic urography, as advocated by Robbins and Hendricks, consisted of a one-eighth inch thick lead sheet fitted under the x-ray tube above the usual aluminum filter. A rectangular opening was cut in the center of the lead sheet so the x-ray beam permitted to pass through the opening was accurately limited to cover only a 14 by 17 inch x-ray film in the table. The size of this opening necessary in the lead sheet on our table (a standard Hugh Young cystoscopic table) was found to measure 3.6 by 4.2 cm.

A simple formula for calculating the diaphragm opening in the lead sheet is noted below:

$$X = \frac{AC}{B}$$

X = the diaphragm opening in one dimension
A = the distance of the radiation source to the diaphragm
B = radiation source to the x-ray plate in the table
C = dimension of the plate in one direction

In review it must be mentioned that a permissible x-ray dose to the urologist should not exceed 150 μr. per week to the hands and 300 μr. total body radiation. From the accompanying drawings of Robbins and Hendricks (Figs. 1, 2 and 3) it is apparent, using the lead sheet diaphragm, that this amount of x-ray will not be available to the examining urologist standing no more than 16 inches from the foot of the table unless he exceeds

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FIG. 1

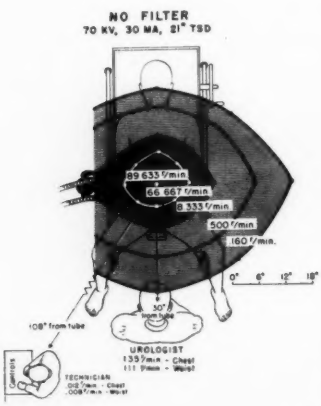


FIG. 2

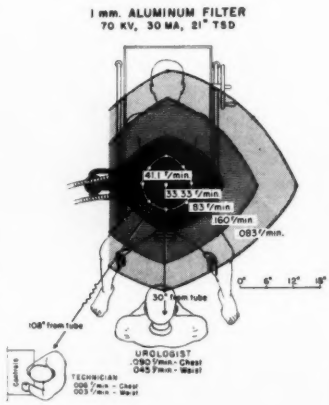
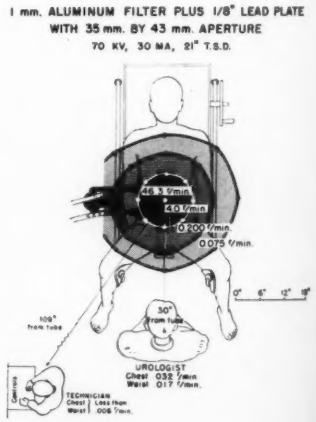


FIG. 3



40 urograms or 120 exposures per week. In our studies, using a direct reading radiation minometer, it was found that the amount of x-ray scatter from the patient and coming into contact with the urologist's hands was slightly in excess of 1 μr. per exposure. Hence, 120 exposures per week provides a most generous factor of safety. It must be stated further that these measurements represent figures calculated for the use of a high speed x-ray screen rather than for par speed. The use of the latter would double the amount of radiation necessary for adequate exposure of the film and hence double the radiation hazard.

The measurement of x-ray penetration of the cystoscopic table was found to reveal an absence of significant penetration at a distance of 25 inches under the table. Therefore, it is apparent that the amount of radiation scatter from the floor is negligible.

Summary

The subject of radiation hazard to the practicing urologist is discussed. The value of a lead diaphragm below the x-ray tube was confirmed to provide the attributes of simplicity and absolute safety.

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Management of Large Benign Tumors of the Rectum*

HERBERT T. HAYES, M.D., HARRY B. BURR, M.D., and
W. TRUETT MELTON, M.D., *Houston, Tex.*

The authors present their thoughts on the local treatment especially of large sessile papillomas or adenomas.

THE MANAGEMENT of large benign polyps of the rectum, particularly those without a pedicle, has always been an interesting and challenging problem. The management of small benign polyps (1 or 2 cm. in diameter) requires only the correct use of the electrocoagulating needle or snare. We should like to suggest that at least a proportion of the larger polyps (over 2 or 3 cm. in diameter) might be eradicated in like manner.

The term "polyp" is inadequate and inaccurate and commonly refers to any benign tumor of the rectum, particularly the pedunculated type. The two most common benign polyps are the adenoma, either pedunculated or sessile, and the papilloma, often called villous papilloma or papillary adenoma.

There is considerable difference between an adenoma and a papilloma as regards origin, histopathology, and potential malignancy. According to Dukes,[1] a lobulated adenoma arises from the glandular epithelial cells lining the mucous glands at the bottom of the crypt of Lieberkuhn. There is a central core or stalk of connective tissue in which blood vessels are present, and a muscularis mucosa that is continuous with the bowel wall; the stalk is covered by columnar epithelium in the form of glands that vary in size and shape. A villous papilloma arises from the surface epithelium, has a broad, sessile base and consists of many finger-like projections, each covered with typical goblet cells of mucosa. The core consists of a connective tissue stroma in which are found small blood vessels and, occasionally, nerve fibers.

We should like to report 5 typical cases of large benign tumors, seen in private practice and to discuss our management.

The occurrence of large adenomas (over 2 or 3 cm. in diameter) of the rectum is relatively rare and poses quite a problem in treatment. Adenomas are usually found at routine examinations while still small, or produce symptoms in the form of a slight amount of blood smeared on, or mixed with the stool. These small tumors are easily destroyed by electrocoagulation. We believe many of the larger tumors may be treated in like manner. One should be extremely hesitant to sacrifice the rectum because of a large benign tumor, although this had to be done in one of our cases because the papilloma filled the entire ampulla and there was no "working room" for the use of an instrument. Bevan's operation, in which the rectum is opened posteriorly for the excision of a benign tumor, may be suitable in rare instances, but must be considered a formidable procedure.

The chief problem before fulgurating a tumor of the rectum is the assurance that the tumor is benign. A good pathologist and several biopsies are mandatory. A biopsy of the surface is of no value. One needs several good bites deep into the substance of the tumor. At times troublesome bleeding is encountered after biopsy; this can be easily controlled with the electrocoagulating needle. Both sessile and pedunculated adenomas frequently present changes in the surface epithelium, such as mitoses, hyperchromaticity or lack of differentiation. This may be interpreted differently by two pathologists. When such changes are present, with invasion and penetration of the muscularis mucosa, definite cancer is present and usually requires radical surgery. As previously emphasized,[2] x-ray examination of the

*Read before the Section on Proctology, Southern Medical Association, Fifty-Second Annual Meeting, New Orleans, La., November 3-6, 1958.

colon should be a routine procedure in all cases of tumor of the rectum.

Technic

The bowel is prepared before operation in an identical manner as though resection and anastomosis were planned—daily laxatives and rectal irrigations, together with nonabsorbable sulfonamides and neomycin by mouth for 4 or 5 days, the latter for 2 days.

The simplest operation is local adequate excision when the lesion is accessible. In 3 of our patients, who had large villous papillomas that could be extruded from the anus, local excision with suture was all that was required. We have not found it necessary to excise through the full thickness of bowel wall and have merely excised the tumor with a cuff of mucosa and submucosa.

Pedunculated polyps can usually be removed with the electrocoagulating snare. The large ones of over 2 or 3 cm. in size may have to be excised piecemeal with the snare. We consider that there are three "musts" in using the snare. First, the pedicle is engaged immediately behind the polyp and not against the bowel wall; second, the engaged portion of polyp is drawn into or against the end of the proctoscope well away from the bowel wall; and, third, the coagulating current is used with low frequency. There is too much danger of penetration of bowel wall if the pedicle is engaged near the wall. When the coagulating current is used and the polyp has been excised, the entire pedicle and 3 or 4 mm. of adjacent mucosa will be whitish, contracted, and completely destroyed so that additional fulguration of the pedicle is unnecessary.

The larger sessile adenomas are destroyed with the electrocoagulating needle and coagulating current. A ball-type electrode which produces only surface coagulation has no place in the treatment of large (or small) adenomas. The needle is thrust through the full-thickness of tumor tissue again and again until the entire tumor is a soft whitish mass. One can be rather bold with the needle since penetration of the bowel wall has not, in our hands, produced any serious complications.

Discussion

We are well aware of the criticism leveled at those who fulgurate rectal tumors and we hope that this discussion will not be considered as a stumbling block in the progress of proctology. Turrell[3] strongly condemns fractional coagulation of adenomas because malignancy in the depths of the tumor may be overlooked. We heartily agree. Having taken several biopsies deep in the tumor before treatment, and having thrust the coagulation needle through the entire thickness of the tumor, this danger is somewhat minimized. Careful frequent follow-up observations are mandatory. If one is as certain as possible that no invasive cancer is present, we think electrocoagulation of large adenomas is preferable to excision through a rectotomy incision with removal of the coccyx as suggested by Best[4] and Miller.[5]

In the recent first edition of "Diseases of the Colon and Rectum," sponsored by the American Proctologic Society, Turnbull[6] reports coagulation of 10 of 21 rectal and colonic polyps in which there was invasive carcinoma. He reports that 9 patients are alive from four to ten years, and one died of myeloma one year later. We cannot endorse this procedure without some reservations. In elderly patients or in those who are extremely poor surgical risks we believe, as do most proctologists, that fulguration of malignant polyps is perfectly "legal" and sensible if we are to serve the best interests of our patients.

One of our patients, 77 years old, lived 5 years after fulguration of an adenocarcinoma 2.5 cm. in diameter on the anterior wall, 4 inches from the anus, and died of other causes. Another patient is alive and well 16 years after fulguration of an adenocarcinoma 5 inches from the anus. We do not recommend routine fulguration of rectal cancer and usually employ radical surgery. However, at times, palliative surgery in the form of electrocoagulation is forced on the surgeon.

It is more than a little embarrassing to remove the rectum after the pathologist reports invasive carcinoma in an excised pedunculated polyp, and have the pathologist report no involvement of the bowel wall at the site of excision. After one or two such experiences, one is inclined to adopt the "wait and see" attitude recommended by Best before advising radical surgery.

Finally, it has been our experience, shared

by every other proctologist, that, as Fansler[7] recently remarked, "surgical operations can never cure all cases of bowel cancer." He was not speaking of electrocoagulation as a surgical procedure. We feel that the latter procedure is preferable in every way to rectotomy incisions with or without removal of the coccyx for large adenomas and, at times, is indicated in frank cancers. If cancer is present, electrocoagulation must be considered a palliative procedure. However, at times a definite cure may be obtained.

Conclusions

1. After several biopsies deep in the substance of a large adenoma, we usually employ electrocoagulation.

2. Surface coagulation is useless. Multiple needle punctures are used in an effort to completely destroy the tumor.

3. Several "sittings" are sometimes necessary to destroy the tumor.

4. Observation at intervals and continued indefinitely are advised. We do not feel too badly about fulgurating small recurrences at the edge of, or in the scar months or years later if repeated biopsies are reported benign. We have never had a cancer develop in such cases.

5. All patients with tumors of the rectum should be subjected to x-ray study of the entire colon before treatment is instituted.

Case Reports

Case 1. Mrs. O. C. B., age 56, had a sessile adenoma on the anterior wall of the rectum beginning at the dentate line, and measuring 2.5 cm. in length and 4 cm. in width. Three biopsies were reported as benign adenoma.

The tumor was fulgurated under saddle-block spinal anesthesia. During the next 3 months small recurrences were fulgurated four times as an office procedure without anesthesia.

Case 2. Mrs. C. W. D., age 42, presented a sessile adenoma on the right wall of the rectum 4 inches from the anus about 2.5 cm. long and 5 cm. wide. Five biopsies were reported as benign adenoma. X-ray examination of the colon was negative.

The tumor was heavily fulgurated under spinal anesthesia 6 years ago. Since that time, tiny to large recurrences in the scar, or at the edge of the scar were fulgurated sixteen times as office procedures. She has been well with no recurrence for one year. Contracture of the scar has narrowed the lumen of the ampulla at the site to about one-half the normal diameter which in no way, interferes with the normal function of the rectum.

Case 3. Mr. J. H. W., age 65, had a lobulated tumor on a short pedicle on the posterior wall 4 inches from the anus. It measured 3 by 2.5 by 2 cm. Two biopsies were reported as benign adenoma and x-ray examination of the colon was negative.

The tumor was removed in segments with the electrocoagulating snare 15 years ago. Except for two small recurrences at the base fulgurated 2 and 3 months after operation, he has been well.

Case 4. Mr. J. L., age 60, had a sessile polyp 5 by 1.5 cm. in size on the right wall of the rectum, just above the dentate line. Biopsy reported a benign papilloma. X-ray study of the colon was negative.

The tumor was excised 5 years ago and there have been no recurrences at the site of removal. A small polyp on the posterior wall 5 inches from the anus was fulgurated one month later.

Case 5. Mr. T. D. S., age 54, presented a sessile tumor 4 cm. in diameter on the right posterior wall about 10 cm. from the anus. Three biopsies were reported as benign. There was another pedunculated tumor 2 cm. in diameter in the sigmoid colon 21 cm. from the anus; x-ray examination of the colon was otherwise negative.

The sessile tumor was fulgurated and the pedunculated tumor removed with the electrocoagulating snare 5 years ago. Three small recurrences in the scar at the site of the sessile tumor were fulgurated 2 and 3 months later and he has remained well since. The pedunculated polyp was benign.

Usually we prefer an abdominal colotomy for pedunculated tumors of the sigmoid because of increased technical problem incident to excision of tumor in that location. However, the man was a poor surgical risk after three coronary occlusions.

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Discussion (Abstract)

Dr. Patrick Hanley, New Orleans, La. I thoroughly enjoyed the presentation of the experiences of Drs. Hayes, Burr and Melton.

Although all surgeons would like to submit to the pathologist the entire specimen of all pathologic lesions, we must guard against doing unnecessary radical excision of benign lesions in order to accomplish this. Many benign lesions can be extirpated by use of conservative procedures.

Our experience with large benign tumors of the rectum has been limited almost entirely to villous

tumors. We prefer to call the villous papillomas and adenomas tumors, for immediately the patient and physician realize that the treatment will be different from that for the usual small benign polyp, which is thought by many to be a simple procedure. As emphasized by Dr. Melton, one must be sure that the tumor is benign. In addition to the multiple biopsies necessary to confirm this, clinically this can be determined by palpation. Benign tumors are soft and velvety. Induration probably indicates malignant degeneration. Fortunately, most large benign villous tumors are located within reach of the palpating finger. Photographs of sagittal sections of fixed villous tumors of the rectum confirm the fact that these are superficial mucosal lesions. Microscopic sections show the many finger-like projections, each covered with typical goblet cells and smooth regular basal membrane.

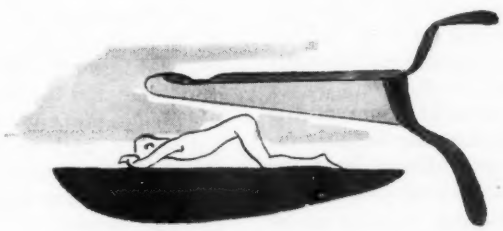
We have never found it necessary to open the rectum posteriorly or to sever the sphincter muscles posteriorly to excise these tumors. We have never used the needle technic as described by Dr. Melton, since we prefer to excise as much of the lesion as we can by multiple biopsies with the large alligator forceps or by electrocautery snare, followed by coagulation with a ball-tipped electrode. All biopsy specimens should be sent to the pathologist for final diagnostic interpretation. Fortunately, most villous tumors are in the lower part of the rectum and the electrocautery snare can be used without too much danger in selected cases. I do not recommend an electrocautery snare for broad-based villous tumors or adenomas above the peritoneal reflection because of the danger of perforation. Lesions above the peritoneal reflection are best treated by anterior resection.

I do not favor coagulation of malignant lesions unless surgical excision is contraindicated. The danger that some large benign villous tumors may have a small malignant area in the base which is not destroyed at the time of coagulation is a point well taken, especially since the villous tumor has a high potential for malignant degeneration. However, we have not hesitated to coagulate large benign villous tumors. We impress upon these patients that the tumor is unusual and has a high incidence of potential malignant degeneration and recurrence, and advise them to return for examination every six months for two years and then yearly thereafter.

I agree with Dr. Melton that the best treatment for tumors of the rectum is surgical excision. I saw a man about 54 years old who had a large villous tumor of the rectum extending from the dentate line to the 8 cm. level. It encircled two-thirds of the circumference of the rectum, beginning in the left posterior lateral aspect and involving all the right side and part of the anterior left side. The posterior and right portions of the tumor were mobile and could be prolapsed through the anus. We decided to excise this in the manner in which we perform radical hemorrhoidectomies. The posterior and right lateral portion of the lesion was excised; however, the mucosa was fixed anteriorly over the surface of the prostate and could not be removed. The remaining portion of the tumor was then destroyed by coagulation.

We have had patients with villous tumors, involving the entire circumference of the rectum and extending 12 to 13 cm. above the dentate line, that could not be destroyed by biopsy and coagulation, because of their enormous size and resultant fibrotic changes. In 7 patients with this type of lesion, resection of the lower part of the rectum was accomplished by performing an abdominal endo-anal pull-through procedure, with preservation of the levator muscles, internal and external sphincter mechanisms, and anastomosis of the upper part of the rectum to the anal skin. This conservative resection of the rectum gives good functional and cosmetic results.

I have enjoyed Dr. Melton's paper and appreciate the privilege of discussing this interesting subject.



EDITORIALS

BROADENING HORIZONS IN PEDIATRIC PRACTICE

First, let me state, that "pediatric practice" as used here, is medical care (preventive and therapeutic) given by both the General Practitioner and the Pediatrician. The designation of "children's doctor" might well apply.

With changing cultural and environmental backgrounds of increased hospital births, urban crowding, ethnic integrations, socio-economic problems, massive movement of families, less family cohesion and many other less well understood situations, emotional and psychological disturbances are admittedly increasing. The present evolutionary development toward a *better standard* of living may well be controversial. Perhaps too far-reaching advances in the sciences of chemistry and physics might be disastrous. At least we do know at this moment that the advances in these two fields have far outstripped our ability to live comfortably with them.

The "children's doctor" has a role in the medical, mental and socio-economic adjustment of the developing children of tomorrow's world. No one of these processes can proceed independently at a pace of its own without collaboration with the other two. The newborn is more and more often deprived of his natural and rightful nutritional needs. There has been, on the other hand, an increasing recognition of his emotional needs in his early hospital stay and his early weeks of home management. The recognition of the importance of this early parent-infant relationship is one segment of the expanding horizon of medical interest. Having this interest in the newborn's adjustment naturally increases the interest of the children's doctor in the child's continuing adaptations during the formative years. As Aristotle so aptly expressed it, "He who sees things from the beginning, has the best view of them."

The continued relationship between physician and child fits the doctor to the task of advising during the adolescent period. The physical, physiological and mental transition to the adult state requires knowledge and understanding. The rebellion against parental restraint, the uncertainty of the future and need for security, as well as the confusion coincident to sex urges, requires cooperation on the part of parent, child and physician. Full use of special services by the doctor is necessary to complete his evaluation and treatment.

These two areas (the newborn and adolescent) of medical care in early life have heretofore received inadequately organized and ineffectual attention in the medical school curriculum and hospital training. Development of the newborn to school age is well known insofar as physical status is concerned, the mental and emotional growth but poorly recognized. The impact of social welfare in the development of human health is inadequately related to education of the students.

The same state exists in the adolescent area. The recognition of "delinquent behavior" has drawn attention to our ignorance of pubescence and its effect on the teen-age youngster floundering in search of stability. It behooves medical schools and teaching institutions to examine their program of instruction and revise it to meet the impacts of new cultural and social changes.

PRESTON A. MCLENDON, M.D.

SCIENCE NEWS

We of the medical profession, who have lived as a doctor for at least twenty years or more, have been keenly aware of a loss of prestige when measured in terms of unquestioned authority, implicit faith and as a reservoir of knowledge of all things medical. From the era of the frock coat, the high hat and the gold headed cane to a matter of a couple of decades ago the doctor's word usually was accepted as gospel, not only in things medical but also in many fields, scientific and educational. In the smaller communities he often was the epitome of the educated and the cultured person.

Many events have conspired to tumble the physician from this pedestal. We are well aware of the socio-economic factors as well as the political, as are pointed up so well by our activities in so-called organized medicine.

There is another factor which is a natural one, not calculated on economic or political grounds. This item is the growing knowledge among the population of things scientific and medical. It is only natural, as mystery is replaced by understanding, that the intelligent person or patient becomes more objective, or at least, the emotional tie between doctor and patient becomes tinged by some degree of objectivity. The doctor is more carefully scrutinized by his patient in terms of newer knowledge, reaction to scientific progress, and its application in practice. Here may be some of the reasons why the patient changes doctors or goes to the neighboring city to consult a self-chosen "specialist."

A most instructive study has appeared as a Report of the National Association of Science Writers, Inc.[1] which throws light on the interests of our population in science news. The survey was made under the financial support of the Rockefeller Foundation, with administrative aid by New York University. The Survey Research Center of the University of Michigan did the work. The technic used was *probability sampling*. Roughly 2,000 American adults were interviewed, each for more than an hour. Science was defined in terms of discoveries in nature, whether in astronomy, atoms, the human body, or in a motor. These topics were divided into "science news" and "medical news."

Picked on percentages, "the 'science reader' is at least a high school graduate. He is in his middle years. He lives in a Western or Middle Western community with a population of between 2,500 and 50,000, or in metropolitan suburbs. He is a white collar worker and earns approximately $5,000 a year." He belongs to several organizations, reads two newspapers daily, subscribes to two or three magazines, listens to the radio an hour or more a day, watches television for a longer time, depending upon the latter media for entertainment and upon his paper and magazines for intellectual fare.

The survey indicated the source from which Americans get their science news. Of the total surveyed, 326 or 17% could recall nothing about science from whatever source during the previous year. Of the remainder, it appeared that the newspapers were the main source of science news, being the primary medium in 41 per cent. Television and magazines came next with 27 and 25% respectively. Radio was the source of news items recalled in only 4 per cent.

It was apparent from this survey that the more knowledge the respondent had on science items, the more media he used in obtaining information. Thus he probably used in addition to the newspapers and magazines the television and/or radio programs.

Women, concerned with the health of the family, read more of the medical news than men who were more interested in the nonmedical science news. Of those who had attended high school, 30% of all males read the medical news and 55% of the women read these items. This degree of interest was less in those who did not go beyond the grade school. Having taken science courses in high school influenced the capacity to remember science news items. With no science courses in high school, 48% of high school graduates could answer three or four questions on science from reading; with exposure to science courses in high school this rose to 62%; and for those with both high school and college science courses recollection rose to 78 per cent.

There was shown to be a greater interest in science news and medical news in the West and Middle West, with less in the South and Northeast. The self-employed and those of better income levels, as might be anticipated from probable educational levels, showed greater interest in "medical" and "science" news.

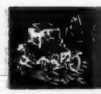
The reading interest in 1957, the time of the study, revealed itself in knowledge of the Salk vaccine, heart disease, cancer, and somewhat in radioactivity as related to health. Many knew of the fluoridation of water supplies.

There is much more in the report of this survey which is interesting and instructive to the scientist and the doctor. It reveals certain facts with which we must reckon. A large segment of our population reads with interest science or medical news items in the newspapers and magazines, and watches programs on television which deal with such subject matter. Many are asking for more of such news at the expense of certain other items

1. Science, The News and the Public. New York, New York University Press, 1958.

in the newspapers. Women particularly wish more medical news. Those with a high school education or more indicate in a goodly proportion a desire for more details in the science or medical news items.

The propaganda value of the newspaper has never been overlooked in the countries of dictatorship. Its impact in science and medical news is apparently very potent. The present-day patient has a nodding acquaintance with things medical. He will therefore look at his doctor more objectively, be more analytical of his methods and practice and will think less of him in terms of a seer or even an authority. Undoubtedly this reading knowledge of things medical is at least one factor influencing the patient-doctor relationship. No matter how much truth there may be in Alexander Pope's line that, "A little learning is a dang'rous thing, . . . ," the intelligent reader patient in 1959 may well be a more questioning soul than the same intelligent patient, but less well read in things medical, of 1929.



25 YEARS AGO

Treatment of Pellagra with Certain Preparations of Liver*

"Many observers have noted that there is a close similarity in the symptoms of pellagra and pernicious anemia of the Addisonian type. However, the skin lesions in the one and the characteristic blood picture in the other serve to differentiate them.

"Goldberger and Sebrell have shown that daily doses of Liver Extract No. 343 by mouth will prevent and cure black tongue in dogs, a disease believed by some to be the analogue of pellagra. Liver and various extracts of liver, therefore, may be suitable agents for a more accurate analysis of the deficiency which brings about pellagra. Our purpose is to record preliminary observations on the effect of an oral and an intramuscular extract of liver in the treatment of pellagra.

"*Method.* If not too far advanced, pellagrins usually recover when brought into a hospital and given a well-rounded diet. To study the effect of the liver preparations it was necessary to prepare a standardized diet similar to that upon which the patient developed the disease. In reviewing the foods consumed by our patients prior to their development of pellagra we were impressed with the similarity between their diets and the diet which Goldberger and Wheeler used in producing pellagra in convicts in Mississippi. In addition to the vitamin G (or B_2) deficiency, Goldberger's original diet was lacking in vitamins A, C and D, and in iron, calcium, phosphorus, and complete proteins. A 2900-calorie diet was prepared consisting of fat meat, field peas, rice, hominy, cane syrup, brown gravy, and lard. To supplement the vitamin, mineral and protein deficiencies already mentioned, the patient received daily 90 cc. of cod liver oil, 45 cc. of tomato juice, 6 Gm. of calcium gluconate, 6 Gm. of iron and ammonium citrate and 60 Gm. of cheese, given as medication on the wards. This diet was called Standard Basic Diet No. 1, being deficient only in vitamin G (or B_2).

"In this study, observations were confined to typical cases of pellagra with skin lesions, sore tongue and gastrointestinal disturbances. A total of 37 patients have been studied in detail, 23 of whom were given the Standard Basic Diet, and the remaining 14 given house diets as controls. . . .

" . . . Three patients, receiving the Standard Basic Diet whose skin lesions had disappeared, were exposed to direct sunlight and developed the characteristic skin rash over the exposed areas. . . .

"*Discussion.* . . . It would seem that the disappearance of the skin lesion does not necessarily indicate a cure of the disease since the lesions can be reproduced by exposure to direct sunlight, unless the patient has been protected by some pellagra-curative substances. The failure of the patient to develop skin lesions after adequate exposure to sunlight furnishes an additional clinical test of the cure of the disease.

"The evidence presented here indicates that the bilateral symmetry of the lesions is due to bilateral exposure to sunlight. In this series it has been shown that unilateral lesions can be produced by unilateral exposure. . . .

"*Summary.* 1. A diet has been prepared for the clinical study of pellagra which is adequate in all known nutritional elements except vitamin G (B_2).

"2. Exposure to direct sunlight in North Carolina in the spring and summer months produces dermatitis in active and potentially active pellagrins, but not in normal controls or in pellagrins who have received adequate treatment.

"3. Ten patients with active pellagra, subsisting upon a basic diet deficient in vitamin G (B_2) showed satisfactory remission after the oral administration of 90 cc. daily of an aqueous extract of liver.

"4. Five patients on the same basic diet showed little or no improvement when given Liver Extract No. 343 intramuscularly in doses of 5 cc. daily. When the oral aqueous extract of liver was substituted for the intramuscular extract, a dramatic clinical improvement began between the 3rd and 5th days and continued until the patients were apparently well."

*Ruffin, J. M., and Smith, D. T.: The Treatment of Pellagra With Certain Preparations of Liver, Am. J. Med. Sc. 187:512, 1934.

SOUTHERN MEDICAL NEWS

ALABAMA

The President of the Southern Medical Association has appointed the following men to serve as Associate Councilors from Alabama: Dr. John M. Chenault, Decatur; Dr. John A. Martin, Montgomery; Dr. W. J. B. Owings, Brent; Dr. John Day Peake, Mobile; and Dr. Buford Word, Birmingham.

ARKANSAS

The President of the Southern Medical Association has appointed the following men to serve as Associate Councilors from Arkansas: Dr. C. Randolph Ellis, Malvern; Dr. Louis K. Hundley, Pine Bluff; Dr. Thomas G. Johnston, Little Rock; Dr. Vincent O. Lesh, Fayetteville; and Dr. Euclid M. Smith, Hot Springs.

The Ouachita County Medical Society has elected as officers: President, Dr. James W. Hawley, Vice-President, Dr. J. B. Jameson, Jr., Secretary, Dr. R. B. Robins, Delegate, Dr. James W. Hawley, all of Camden; and Alternate Delegate, Dr. Bruce Ellis, Stephens.

Dr. Paul Ledbetter, Jonesboro, was recently elected President of the Craighead-Poinsett Medical Society. Other officers elected were: Dr. C. Z. Swingle, Marked Tree, Vice-President; and Dr. J. H. McCurry, Cash, Secretary.

Dr. Ramond E. Peeples, Malvern, has given up his practice to accept a Fellowship for specialization in anesthesia. Dr. Peeples entered New Orleans Charity Hospital in January. He will also serve on the staffs of both Tulane and Louisiana State University.

DISTRICT OF COLUMBIA

Dr. Milford O. Rouse, Dallas, Texas, President of the Southern Medical Association, has appointed the following physicians to serve as Associate Councilors from the District of Columbia: Dr. William P. Herbst, Dr. Oscar Benwood Hunter, Jr., Dr. Preston A. McLendon, and Dr. Margaret M. Nicholson.

Dr. Murray M. Copeland, Director, Department of Oncology, Georgetown University School of Medicine, was recently elected Chairman of the Joint Committee for Cancer Staging and End Results Reporting.

Dr. Desmond S. O'Doherty, Associate Professor of Neurology in the Georgetown University School of Medicine, has taken over the duties of Dr. Francis M. Forster in the direction of the Department of Neurology. Dr. Forster, Chairman of the Department and former Dean of the Medical School, has resigned to accept a position as Director of the Department of Neurology at the University of Wisconsin, Madison.

FLORIDA

The President of the Southern Medical Association has appointed the following men to serve as Associate Councilors from Florida: Dr. Edwin H. Andrews, Gainesville; Dr. Charles McC. Gray, Tampa; Dr. Francis T. Holland, Tallahassee; Dr. George W. Morse, Pensacola; and Dr. G. Dekle Taylor, Jacksonville.

Dr. Geoffrey H. Binneveld, Leesburg, has been elected Vice-President of the Lake County Unit of the American Cancer Society.

The following county medical societies have elected officers:

Bay County. Dr. James D. Nixon has been elected President; Dr. John J. Hollman, Jr., Vice-President; Dr. Robert L. Overman, Secretary; and Dr. Charles H. Daffin, Treasurer. All are from Panama City.

Brevard County. Dr. Louis C. Jensen, Jr., Rockledge, President; and Dr. Carl J. Arnold, Jr., Cocoa, Secretary-Treasurer.

Collier County. Dr. John J. Meli, President; Dr. Loral F. Gwaltney, Vice-President; Dr. William J. Bailey, Treasurer; and Dr. Ethel H. Trygstad was re-elected Secretary. All are from Naples.

Columbia County. Dr. Harry S. Howell, President; Dr. Louis G. Landrum, Vice-President; and Dr. Thomas H. Bates, Secretary-Treasurer, all of Lake City.

DeSoto-Hardee-Highlands-Glades County. Dr. James G. Smith, President; Dr. Merle C. Kayton, Vice-President; and Dr. Miles A. Collier, Secretary-Treasurer, all of Wauchula.

Escambia County. Dr. Egbert V. Anderson, Pensacola, President; Dr. William J. Overstreet, Warrington, President-Elect; Dr. Joseph L. Rubel, Pensacola, Vice-President; and Dr. Joseph Q. Perry, Pensacola, Secretary-Treasurer.

Hillsborough County. Dr. Harold G. Nix, President; Dr. Linus W. Hewitt, President-Elect; Dr. James A. Winslow, First Vice-President; Dr. Hugh G. Steele, Second Vice-President; and Dr. Collin F. Baker, Jr., Secretary, all of Tampa.

Jackson-Calhoun County. Dr. Glenn E. Padgett, President; Dr. Courtland D. Whitaker, Vice-President; and Dr. Francis M. Watson, Secretary-Treasurer. All are from Marianna.

Lake County. Dr. Frederick C. Andrews, Mount Dora, President; Dr. Lawton F. Douglass, Umatilla, Vice-President; and Dr. Thomas D. Weaver, Clermont, Secretary-Treasurer.

Marion. Dr. Earl E. Yantis, President; Dr. Robert L. Gibson, Vice-President; and Dr. Wallace E. Winter, Secretary-Treasurer. All are from Ocala.

Monroe. Dr. Joseph J. Scarlet, President; Dr. Walter R. McCook, Vice-President; and Dr. Herman K. Moore, Secretary-Treasurer, all of Key West.

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Dr. Milford O. Rouse, Dallas, Texas, President of the Southern Medical Association, has appointed the following men to serve as Associate Councilors from Georgia: Dr. Edgar Boling, Atlanta; Dr. T. Luther Byrd, Atlanta; Dr. Hugh B. Cason, Warrenton; Dr. Walker L. Curtis, College Park; and Dr. C. H. Richardson, Jr., Macon.

The following County Medical Societies have elected officers:

Bartow County. President, Dr. A. L. Horton; Dr. W. B. Quillion, Vice-President; and Dr. Thomas Hamilton, Secretary-Treasurer, all of Cartersville.

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KENTUCKY

Dr. Milford O. Rouse, Dallas, Texas, President of the Southern Medical Association, has appointed the following men to serve as Associate Councilors from Kentucky: Dr. G. Y. Graves, Bowling Green; Dr. O. Leon Higdon, Paducah; Dr. Sam A. Overstreet, Louisville; Dr. Charles C. Rutledge, Hazard; and Dr. Carroll L. Witten, Louisville.

Dr. Carroll L. Witten, Louisville, section officer on General Practice in the Southern Medical Association, and Chairman of the Kentucky State Medical Association School Health Committee, has been elected Chairman of the Kentucky School Health Council. Dr. Judith A. Stout, State Department of Health, Louisville, was elected Secretary.

Dr. George W. Pedigo, Jr., Louisville, Associate Editor of the *Journal of the Kentucky State Medical Association,* has been chosen President-Elect of the Jefferson County Medical Society. Other officers elected at the annual meeting are: Dr. Daniel G. Costigan, First Vice-President; Dr. Roy A. Martin, Second Vice-President; Dr. Maurice T. Fliegelman, Secretary; Dr. Max P. Jones, Treasurer; and Dr. J. Thomas Giannini and Dr. Thomas M. Marshall, Judicial-Council members, all of Louisville.

Members appointed to the Kentucky State Medical Association Advisory Commission to Blue Shield are: Dr. W. Vinson Pierce, Covington, Chairman; Dr. C. Walker Air, Covington; Dr. Harry S. Andrews, Louisville; Dr. Chester M. Blanton, Paducah; Dr. Willard Buttermore, Corbin; Dr. Louis M. Foltz, Louisville; Dr. Hugh Houston, Murray; Dr. Arthur H. Keeney, Louisville; Dr. J. Murray Kinsman, Louisville; Dr. James T. McClellan, Lexington; Dr. William K. Massie, Lexington; Dr. Alfred O. Miller, Louisville; Dr. Robert A. Orr, Mayfield; Dr. Sam A. Overstreet, Louisville; Dr. Richard R. Slucher, Louisville; Dr. Garnett J. Sweeney, Liberty; Dr. Malcolm D. Thompson, Louisville; Dr. Donald B. Thurber, Louisville; Dr. William R. Willard, Lexington; and Dr. Fred M. Williams, Louisville. Drs. Pierce, Air, Andrews, Miller, Slucher, Thompson, and Willard make up the Executive Committee of the Commission.

Dr. R. Lee Walton, former instructor at Yale University Medical School, has been appointed to the newly created position of Pediatric Consultant in the Bureau of Maternal and Child Health Department of the State Department of Health, according to Dr. Russell E. Teague, Commissioner of Health.

Dr. R. J. Ritterhoff, Covington, was elected President of the Kentucky Society of Pathologists at a meeting at the Lexington Clinic. Other officers include: Dr. John D. Allen, Louisville, President-Elect; and Dr. H. Davis Chipps, Lexington, Secretary-Treasurer.

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BOOKS RECEIVED

Breast Cancer. Edited by Albert Segaloff, M.D., Director of Endocrine Research, Alton Ochsner Medical Foundation, Associate Professor of Clinical Medicine, Tulane University School of Medicine. 239 pages. St. Louis: The C. V. Mosby Company, 1958. Price $5.00.

The Practice of Sanitation. By Edward Scott Hopkins, Principal Associate Engineer, Bureau Water Supply, Baltimore, Maryland (Ret.); and Wilma Henry Schulze, Assistant Commissioner of Health, Sanitary Section, Baltimore City Health Department. Third Edition, 473 pages. Baltimore: The Williams & Wilkins Company, 1958. Price $8.00.

The Recovery Room. By John Adriani, M.D., Professor of Surgery, Tulane University School of Medicine; and John B. Parmley, M.D., Instructor in Surgery, Tulane University School of Medicine. 123 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $4.50.

Amid Masters of Twentieth Century Medicine. By Leonard G. Rowntree, M.D. Chairman, Medical Advisory Board, The American Legion. Chairman, Dean's Committee, V. A. Hospital, Coral Gables; Co-Founder, University of Miami School of Medicine. 683 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $11.50.

Pain. By Harold C. Wolff, M.D., Professor of Medicine (Neurology), Cornell University Medical College, New York City; and Stewart Wolff, M.D., Professor and Head, Department of Medicine, Oklahoma City, Okla. 121 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958.

Handbook of Balanced Anesthesia. By Sylvan M. Shane, Attending Anesthesiologist, Lutheran Hospital of Maryland; Chief of Anesthesiology, Doctors Hospital of Baltimore; Consultant in Anesthesiology, Spring Grove Hospital of The State of Maryland; formerly, Anesthesiologist at the Baltimore City Hospitals, The Southern Baltimore General Hospital, and The Baltimore Eye, Ear, and Throat Hospital. 260 pages. Baltimore: Lowry & Volz, 1958. Price $7.85.

Diseases of Children in the Subtropics and Tropics. By H. C. Trowell, M.D., Senior Specialist Physician, Paediatric Unit, Mulago Hospital and Makerer College, University College of East Africa, Kampala, Ugando; and D. B. Jelliffe, M.D., Visiting Professor of Tropical Medicine, Tulane University, New Orleans, La. 901 pages. London: Edward Arnold, Publisher, Ltd., 1958. Price $18.50.

Neurological Basis of Behavior. Ciba Foundation Symposium. Edited by G. E. W. Wolstenholme and Cecilia M. O'Connor. 387 pages, with 109 illustrations. Boston: Little, Brown and Company, 1958. Price $9.00.

Water and Electrolyte Metabolism in Relation to Age and Sex. Edited by G. E. W. Wolstenholme and Maeve O'Connor. Ciba Foundation Colloquia on Ageing, Vol. 4. 317 pages, with 85 illustrations. Boston: Little, Brown and Company, 1958. Price $8.50.

Clinical Endocrinology. By Karl E. Paschkis, M.D., Associate Professor of Medicine and Associate Professor of Physiology; Abraham E. Rakoff, M.D., Clinical Professor of Obstetrics and Gynecologic Endocrinology; and Abraham Cantarow, M.D., Professor of Biochemistry, all of Jefferson Medical College, Philadelphia. 880 pages, with 274 illustrations, 6 in color. New York: Paul B. Hoeber, Inc., 1958. Price $18.00.

The Neurologic Examination. By Russell N. DeJong, M.D., Professor of Neurology and Chairman of Department of Neurology, University of Michigan Medical School. Second Edition, 1,039 pages, with 368 illustrations. New York: Paul B. Hoeber, Inc., 1958. Price $20.00.

Obstetrical Practice. By Alfred C. Beck, M.D., Professor Emeritus of Obstetrics and Gynecology; and Alexander H. Rosenthal, M.D., Clinical Associate Professor of Obstetrics and Gynecology, both of State University of New York College of Medicine. Seventh Edition, 1,069 pages. Baltimore: The Williams & Wilkins Company, 1958. Price $14.00.

Systemic Ophthalmology. Edited by Arnold Sorsby. Second Edition, 682 pages. St. Louis: The C. V. Mosby Company, 1958. Price $25.00.

Callander's Surgical Anatomy. By Barry J. Anson, Ph.D., Chairman, Department of Anatomy; and Walter G. Maddock, M.D., Edward S. Elcock, Professor of Surgery, both of Northwestern University Medical School. Fourth Edition, 1,105 pages, with 1,047 illustrations. Philadelphia: W. B. Saunders Company, 1958.

A Classified Bibliography of Gerontology and Geriatrics. Supplement One 1949-1955. By Nathan W. Shock, Chief, Gerontology Branch, National Heart Institute. 442 pages. Stanford, Calif.: Stanford University Press, 1957. Price $15.00.

Radioactive Isotopes in Clinical Practice. By Edith H. Quimby, Sc.D., Professor of Radiology (Physics); Sergei Feitelberg, M.D., Clinical Professor of Radiology; and Solomon Silver, M.D., Associate Clinical Professor of Medicine, all of the College of Physicians and Surgeons, Columbia University. 451 pages, 97 illustrations. Philadelphia: Lea & Febiger, 1958. Price $10.00.

An Introduction to Physics in Nursing. By Hessel Howard Flitter, R.N., Assistant Director, Test Construction Unit, National League for Nursing. Third Edition, 242 pages. St. Louis: The C. V. Mosby Company, 1958. Price $3.75.

Physiology of Prematurity. Transactions of the Second Conference, March, 1957. Edited by Jonathan T. Lanman, M.D., Department of Pediatrics, New York University-Bellevue Medical Center. 150 pages. New York: Josiah Macy, Jr. Foundation, 1958. Price $3.75.

Bacterial and Mycotic Infections of Man. Edited by Rene J. Dubos, Ph.D., The Rockefeller Institute. Third Edition, 796 pages, 116 illustrations. Philadelphia: J. B. Lippincott Company, 1958. Price $8.50.

The Practical Use of the Microscope. By George H. Needham, M.S., Lecturer in Microscopy and Photomicrography, University of California Medical School. 473 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $15.50.

Infectious Diseases of Children. By Saul Krugman, M.D., Associate Professor of Pediatrics, New York University College of Medicine; and Robert Ward, M.D., Professor and Head of the Department of Pediatrics, University of Southern California. 330 pages with 44 illustrations and 7 color plates. St. Louis: The C. V. Mosby Company, 1958. Price $10.00.

INSTRUCTIONS TO CONTRIBUTORS

Exclusive Publication: Articles offered for publication must be contributed solely to the Southern Medical Journal.

Manuscripts: Manuscripts should be original copy, typewritten, double-spaced, with wide margins. Because of lack of space, it is necessary to limit the number of bibliographic references to twenty. Footnotes and references should conform to the following style:

1. Doe, J. E.: What You Should Know about It, New England J. Med. 243:435, 1950.

Illustrations: Black and white glossy prints, preferably 5 by 7 inches, and drawings in India ink on white paper are required. The author's name, number and indication of top, if doubtful, should be attached. Necessary plates not exceeding six, or one and a half pages, will be furnished by the Journal.

Reprints: Reprints are available at publisher's cost. An order form will accompany author's galley proof and should be returned with the galley to the Editor.

Book Reviews: Books and monographs submitted for review should be mailed to the Editor. Acknowledgment will appear in the Journal. Selection rights reserved.

Editorial Address: All manuscripts, corrected galley proof, reprint orders, books for review and related correspondence should be addressed to the Editor, R. H. Kampmeier, M.D., Vanderbilt University School of Medicine, Nashville 5, Tennessee.

Business Address: All correspondence related to membership, subscriptions, advertising, and other business should be addressed to the Southern Medical Association, 2601 Highland Avenue, Birmingham 5, Alabama.

BOOK REVIEWS

The Human Ear Canal

By Eldon T. Perry, M.D., Instructor in Dermatology, Wayne University. American Series No. 322. 107 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1957. Price $4.75.

The human ear canal has presented problems of diagnosis and treatment to otolaryngologists and dermatologists for many years. There has been a great deal of controversy about the cause or causes of external otitis. Fungus disease was commonly accepted as the etiologic factor by many workers until recently.

This excellent book systematically by means of cultures, histopathology and pertinent experiments, lays the ground work for a better understanding of external otitis. It places bacteria and fungi in their proper perspective and develops a logical approach to the diagnosis and treatment.

Although the differential diagnosis is not given in detail, the various generalized dermatoses like psoriasis, seborrheic dermatitis, neurodermatitis, etc. are described and signs are given leading to their proper diagnosis.

This book should be valuable to all physicians who treat external otitis and should be available as a reference text in libraries.

Adventures in Medical Education

By G. Canby Robinson, M.D., 338 pages. Cambridge, Mass.: Published for the Commonwealth Fund by Harvard University Press, 1957. Price $5.00.

Dr. Robinson has written a personal narrative of the great social and medical revolution which has taken place during the past 50 years. He has had a varied experience and a unique opportunity to take part in events of great importance during the growth of medicine, which raised the standards of medical education to the university level.

The first part of his book deals with the early growth of medical education, from its first beginning in Colonial days, when doctors were trained as apprentices. Of interest are the prophets of organized medical education, who pointed the way, should lead American medicine toward the highest place in the world today. In this group are Dr. John Morgan, who received the first academic appointment in 1765 as Professor of Medicine at the College of Philadelphia —Dr. Patrick Macaulay, the first to plead for hospital teaching facilities, essential for medical education, and the stormy and influential career of Dr. Daniel Drake, who pioneered the development of medical education in the Ohio Valley.

The main portion of the book begins with the founding of the medical school of the Johns Hopkins University in 1893. There for the first time in this country, medicine was taught at the true university level to students who were college graduates with special training in the natural sciences and modern languages.

Dr. Robinson's personal adventures in medical education start with an account of his entrance to medical school at Johns Hopkins in 1899, and from his experiences, we are able to see how medical research developed in this country, and how modern medicine spread to the Middle West at Washington University, to the South at Vanderbilt University, to New York at Cornell, and the New York Hospital and later developed in China at the Peiping Union Medical College.

Principles of Internal Medicine

Editors: T. R. Harrison, Raymond D. Adams, Ivan L. Bennett, Jr., William H. Resnik, George W. Thorn, and M. M. Wintrobe. Third Edition, 1,782 pages. New York: McGraw-Hill Book Company, Inc., 1958. Price $18.50.

At the time of this third edition it is hardly necessary to call attention to its excellence as a textbook in medicine or to comment upon the many authorities who contribute the content of this text. The first two editions established this book as an authoritative work, and this reviewer's comment can only re-emphasize these points in the belief that this is the outstanding reference work in the field today.

Naturally, progress has been made in the medical field since the second edition went to print, and this accounts for the need of a new edition and revision of certain portions of the text. The new topics which appear in the book are several. Advances in knowledge with regard to the functions of circulatory and respiratory systems have required a revision of former writings. So too, increasing knowledge with regard to ACTH and steroids has required an extension of the portions dealing with these substances. The section on diseases of the nervous system has been rewritten and place has been given to the drugs which now are available for the treatment in psychiatric diseases.

Again the reviewer emphasizes the position this textbook holds as the outstanding one in its field.

Fundamentals in Cardiology

By John B. Wild, M.D., Assistant Professor, Department of Internal Medicine, University of Iowa, Iowa City. 80 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $4.50.

This handy little book is a successful integration of the electrical, pressure, flow and sonic events in the beating heart. The author uses a clear writing style and excellent diagrams to show the interrelationships, first in the normal heart and then in hearts with single major valvular defects. The publisher will help this effort in subsequent editions if he arranges the text to face the pertinent illustration. These are presently often out of phase.

The discussion of the abnormal sounds associated with mitral stenosis is especially well done. The origins of a split second, an opening snap and a loud first sound are lucidly discussed. Whether these origins are correctly ascribed or not, the author makes clear how they can usually be discriminated. All these matters, having assumed a new importance with the ad-

vent of corrective heart surgery, are worth reviewing and this little book offers a good way to do it.

The Dermatologist's Handbook

By Ashton L. Welse, M.D., Assistant Professor of Dermatology and Syphilology, University of Cincinnati College of Medicine. 396 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1957. Price $15.00.

The author states in the preface to this volume: "The objective which prompted preparation of this handbook was: Organization into a rational systematic classification, for purposes of instruction and reference, that large number of topical and internal therapeutic agents concerning which a dermatologist must have knowledge."

This large book of 396 pages is certainly comprehensive, but even so does not include every product of every distributor.

The author is recognized as an enthusiastic therapist, who liberally prescribes local and internal medication. Some may wonder whether all his enthusiasm is justified by the results.

Likewise, one wonders whether this large book which attempts to be comprehensive, yet is not complete, serves any essential purpose.

The Preservation of Youth. Essays on Health

Translated from Original Arabic with Introduction by Hirsch L. Gordon, M.D. 92 pages. New York: Philosophical Library, 1958. Price $2.75.

The great philosopher and physician, Maimonides (Moses ben Maimon), was consulted in 1198 by Sultan Al Afdal for certain advice as to rules of living. Maimonides report, "The Preservation of Youth," written originally in Arabic, was later translated into Hebrew in 1244, into Latin in 1290 and used extensively in the medical schools of Europe. This present volume is the first English translation.

This small volume is crowded with sound advice the more remarkable, as one remembers it is a 12th century edition. The teachings are by and large current and modern. Particularly advice is given about diet, exercise, constipation, intercourse, and sleep. Of interest is his statement, "The ignorant say that medicine is just a profession, that one can learn it through exercise—the more perfect a person becomes in one of the sciences, the more cautious he grows—and the more deficient one is in science, the easier it will be for him to understand every difficulty, making the improbable probable, and increasing the false claims which he represents as certain knowledge, and is eager to explain things that he does not understand himself."

Handbook of Treatment of Acute Poisoning

By E. H. Bensley, Associate Professor of Medicine and Lecturer in Toxicology, McGill University; and G. E. Joron, M.D., Demonstrator in Medicine, McGill University, Montreal. 206 pages. Baltimore: The Williams and Wilkins Co., 1958. Price $4.00.

This small volume on acute poisoning contains two sections. The first is intended to "help physicians with no special experience in toxicology when called upon suddenly and unexpectedly to treat cases of acute poisoning." This section, which takes up the first 38 pages of the volume, accomplishes this purpose in a very concise fashion. It is perhaps a trifle repetitious, but this can be condoned on the basis that the information necessary must be readily available. The second section is devoted to the specific treatment of poisoning by many common agents and is designed for handy rapid reference. It may also be used as the "basis of a course in the management of acute poisoning for students of medicine." This section is remarkably concise and up to date. The judgment used in the selection of the poisons to be covered is admirable.

In view of the fact that accidental ingestion of poisons is reasonably common in children, it is regretted that accurate doses of the various antitoxins and medications used are not outlined for children. This book does not make any effort to answer the question which so frequently confronts the physician when the brand name of the ingested substance is known; therefore this volume cannot be, and is not intended to be, a complete guide for the treatment of poisoning.

Rypins' Medical Licensure Examinations

By Walter L. Bierring, M.D., with collaboration of a Review Panel. Eighth Edition, 943 pages. Philadelphia: J. B. Lippincott Company, 1957. Price $10.00.

As with previous editions this book is designed especially for those preparing for medical qualifying examinations. The text is divided into two parts: Basic sciences and clinical sciences. Following each chapter is a large list of questions which serve as an excellent method of review.

All sections are up-to-date despite the shortcomings of brevity seen under Medicine and Surgery. As in previous editions, there are no diagrams, and but few tables. The Section on Psychiatry contains a large glossary of psychiatric terms and little else.

The reviewer actually used this book in preparing for a State Board Examination and found it quite useful.

Epilepsy Handbook

By Frederic A. Gibbs, M.D., Professor of Neurology, University of Illinois School of Medicine; and Frederick W. Stamps, M.D., University of Illinois School of Medicine. 92 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $4.75.

The authors, who have had considerable experience in the diagnosis and treatment of epilepsy, have written a very succinct and informative handbook. After a brief preliminary discussion regarding the definition and etiology of this disorder, the various types of epilepsy are defined with respect to the clinical manifestations, the electroencephalographic changes and therapy. Subsequent chapters deal with differential diagnosis and the available anticonvulsant preparations. The appendix contains an excellent summary in table form.

A very commendable feature of this volume is a colored plate in which the dosage forms of the anticonvulsant medications are depicted in natural color and size. This should be very useful to all physicians in reviewing the history of previous medication with their patients.

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*Dr. T. Oscar Vinson, *Secretary*, Director, De Kalb County Health Department, 126 Trinity Place, Decatur, Georgia

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Dr. J. Maxey Dell, Jr., *Vice-Chairman*, 217 S. Main Street, Gainesville, Florida

*Dr. Seymour Ochsner, *Secretary*, Ochsner Clinic, 3503 Prytania Street, New Orleans 15, Louisiana

Section on Surgery

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*Dr. Guy W. Horsley, *Vice-Chairman*, 617 W. Grace Street, Richmond 20, Virginia

*Dr. M. L. Michel, *Secretary*, 1441 Delachaise Street, New Orleans 15, Louisiana

Section on Urology

Dr. H. King Wade, Jr., *Chairman*, 231 Central Avenue, Hot Springs, Arkansas

*Dr. Max Mayo Green, *Vice-Chairman*, 4440 Magnolia Street, New Orleans 15, Louisiana

*Dr. William H. Morse, *Secretary*, 188 So. Bellevue Street, Memphis 4, Tennessee

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*New Officers—Elected New Orleans Meeting, 1958.

BOOK REVIEWS

Continued from page 495

This book will be of value to students and practitioners. It deserves a place in all medical libraries.

The Practical Use of the Microscope

By George H. Needham, M.S., Lecturer in Microscopy and Photomicrography, University of California Medical School. 473 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $15.50.

Here in one convenient volume is a rich reference source for all phases of microscopy. The author concisely discusses the principles of the many different types of microscopes and how to use them. There are included chapters on illumination, filters, micrometry, microprojection and photomicrography. There is also a valuable appendix containing conversion factors, tables of refractive indices, microscope manufacturers and photomicrographic equipment.

Medical Electrical Equipment. Principles, Installation, Operation and Maintenance of Electrical Equipment Used in Hospitals and Clinics

Advisory Editor, Robert E. Molloy, M.B. 306 pages, 238 illustrations. New York: Philosophical Library, Inc., 1958. Price $15.00.

Apparently this book was originally published in England for use in the United Kingdom.

It should prove an excellent handbook for our counterparts of the British Empire. However, the terminology may seem strange to the American technician. The equipment used for illustration is basically similar to that used in the U.S.A. However, the physical appearance and often the values of voltage, current, and frequency are quite different.

If one is willing to ignore these discrepancies, it does present a wealth of information which should be useful in any hospital, provided, of course, one is familiar with the electrical standards and regulations for his location.

Liver, Biliary Tract and Pancreas. Part III of Volume 3. Digestive System, The Ciba Collection of Medical Illustrations

By Frank H. Netter, M.D. 149 pages. Summit, New Jersey: Ciba, 1957. Price $10.50.

As in similar volumes published by Ciba in the past few years, this consists of a compilation of colored drawings of normal and pathologic states. A short explanation accompanies the illustrations, by well known authorities in their particular fields. The illustrations deal with the normal anatomy and physiology of the organs considered, as well as the patho-physiology of disease, in the liver, gallbladder and pancreas.

This type of volume offers a ready reference work to the busy doctor, and the reviewer has often found the Ciba collection of medical illustrations a handy teaching tool for intelligent and interested laymen and patients.

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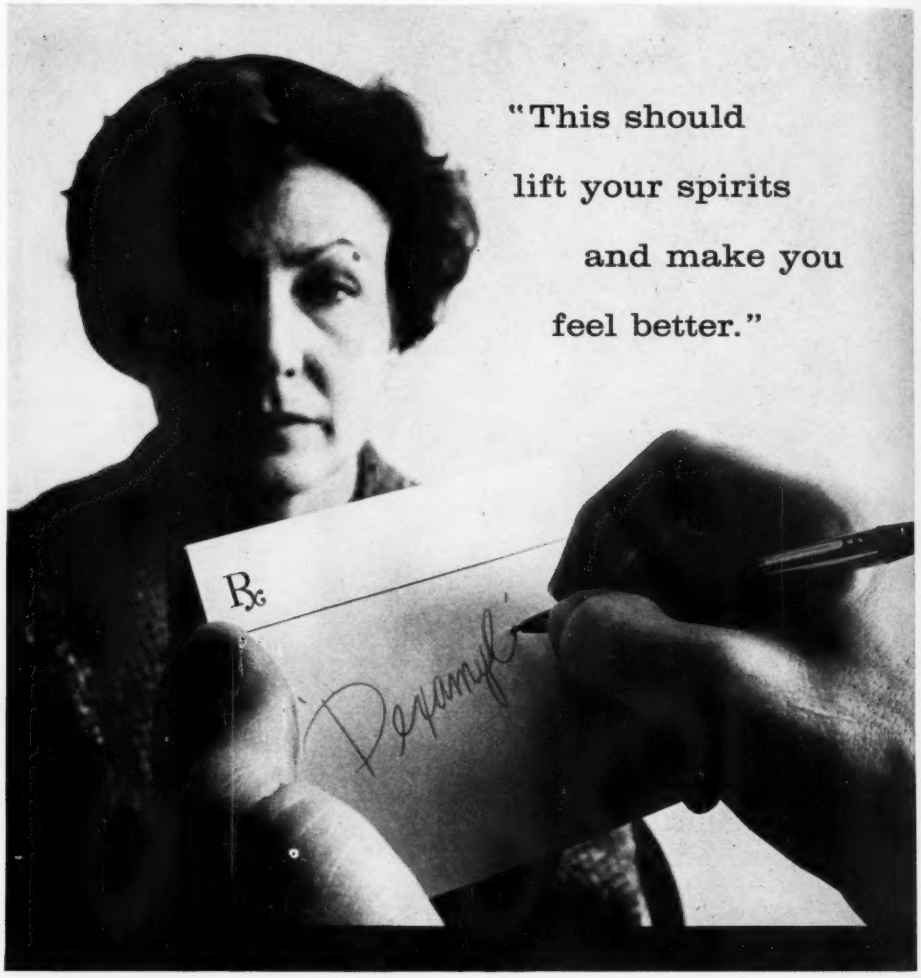

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Nasal Solution, 1/2-oz. dropper bottle, 0.1%. Each cc. contains 1 mg. tetrahydrozoline hydrochloride, 0.2 mg. prednisolone, and 0.6 mg. neomycin (as sulfate).

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Note: As with certain other widely used nasal decongestants, overdosage may cause undesirable effects, especially deep sleep in infants and young children; hence, use of adult strength drops in children under six years of age is not recommended. Use Pediatric Nasal Drops (0.05%) for children under six years. When Tyzine Nasal Spray is administered, it should be held only in an upright position.

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NEW PRODUCT ANNOUNCEMENT

Continued from page 492

LOUISIANA

The President of the Southern Medical Association, Dr. Milford O. Rouse, Dallas, Texas, has appointed the following men to serve as Associate Councilors from Louisiana: Dr. C. E. Boyd, Shreveport; Dr. Humphrey H. Hardy, Jr., Alexandria; Dr. Henry W. Jolly, Jr., Baton Rouge; and Dr. George W. Wright, Monroe.

Dr. Paul C. Beaver, Tulane School of Medicine, has been appointed the William Vincent Professor of Tropical Diseases and Hygiene at Tulane Medical School. Dr. Beaver, formerly Professor of Parasitology, has been a member of the medical school faculty since 1945. He succeeds Dr. Ernest Carroll Faust, who has reached retirement age but continues as field coordinator of the Tulane Consultant Program with the seven medical schools of Colombia, South America.

The following officers have been elected by the Calcasieu Parish Medical Society: President, Dr. E. C. Campbell; Vice-President, Dr. W. M. Farmer; Secretary, Dr. J. M. Swain; and Treasurer, Dr. L. M. Warshaw, all of Lake Charles.

Dr. Alton Ochsner, New Orleans, has been elected an Honorary Life Member of the Board of Directors of the American Cancer Society, and to honorary memberships in the Nassau Surgical and Mississippi Valley Medical Societies.

Dr. Irwin M. Marcus, New Orleans, was recently elected by the Governing Council of the Society for Research in Child Development to serve as Consulting Editor for their national publication.

MARYLAND

Dr. Milford O. Rouse, Dallas, Texas, President of the Southern Medical Association, has appointed the following men to serve as Associate Councilors from Maryland: Dr. Francis A. Ellis, Baltimore; Dr. Robert E. Ensor, Towson; Dr. E. Paul Knotts, Denton; and Dr. J. Morris Reese, Baltimore.

Dr. Dick W. T. Wei, Baltimore, has been elected to membership in the American Society of Anesthesiology.

New officers of the Prince George's County Medical Society are: President, Dr. David S. Clayman, Riverdale; Vice-President, Dr. John S. Haught, Mt. Rainier; Secretary, Dr. R. D. Bauer, Adelphi; and Treasurer, Dr. Albert Roth, Riverdale.

The following officers have been elected by the Medical Staff of the Anne Arundel General Hospital, Annapolis: President, Dr. Manning W. Alden; Vice-President, Dr. Edward S. Beck; and Secretary, Dr. Richard N. Peeler.

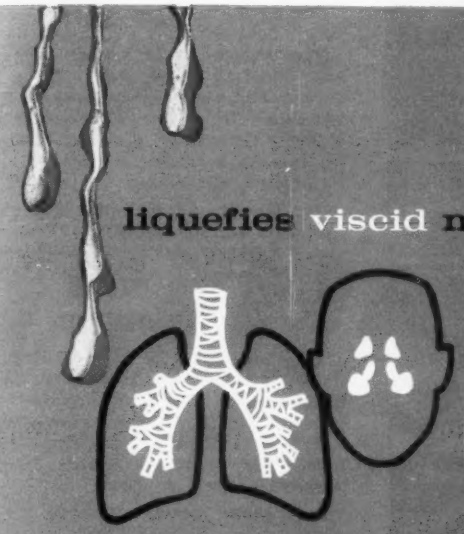
Dr. Edward A. Kitlowski, Baltimore, was named to receive the 1958 Physicians' Award by the Governor's Committee to Promote the Employment of the Physically Handicapped.

The American Venereal Disease Association will hold its annual meeting April 27 and 28 in the Auditorium of Johns Hopkins Hospital, Baltimore, in co-sponsorship with the United States Public Health Service of the Tenth Annual Symposium on Recent Advances in the Study of Venereal Diseases.

Continued on page 72

NEW USE

CHYMAR® Aqueous
Chymotrypsin



in asthma, bronchitis, rhinitis and sinusitis

Chymar Aqueous was used as adjunctive therapy for 60 patients suffering from asthma, bronchitis, rhinitis or sinusitis. "In the majority (48) of these cases, improvement was demonstrated by easier breathing, improved vital capacity, thinning of bronchial secretions, ability to raise sputum more freely and a reduction in the amount of expectoration."[1] In 2 other studies, Chymar was used with good success in treating 45 cases of asthma.[2,3] Supplied in 5 cc. multiple dose vials with 5000 Armour Units per ml. Also available as Chymar in Oil. 1. Parsons, D. J.: *Clinical Medicine* 5:1491, 1958. 2. Diaz, E. S.: *Revista de la Confederacion Medica Panamericana* 5:402, 1958. 3. Diaz, E. S.: *Sinopsis Medica Internacional* 6:20 (March) 1958.

Chymar Aqueous is also preferred for systemic anti-inflammatory action in obstetrics, gynecology, dermatology, surgery, accidents and eye diseases.

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Continued from page 70

The Allegany-Garrett County Medical Society has elected as officers: Dr. Leland B. Ransom, President; Dr. Leslie E. Daugherty, Vice-President; Secretary, Dr. Carlton Brinsfield; and Treasurer, Dr. Thomas F. Lewis, all of Cumberland.

MISSISSIPPI

The President of the Southern Medical Association, Dr. Milford O. Rouse, Dallas, Texas, has appointed the following men to serve as Associate Councilors from Mississippi: Dr. Eldon L. Bolton, Biloxi; Dr. Jesse T. Davis, Corinth; Dr. Raymond F. Grenfell, Jackson; Dr. Howard A. Nelson, Greenwood; and Dr. Robert E. Schwartz, Hattiesburg.

Dr. William C. Holland, Vanderbilt University School of Medicine, Nashville, Tennessee, has been named Professor of Pharmacology and Chairman of the Department at the University of Mississippi School of Medicine.

MISSOURI

The President of the Southern Medical Association, Dr. Milford O. Rouse, Dallas, Texas, has appointed the following men to serve as Associate Councilors from Missouri: Dr. A. Graham Asher, Kansas City; Dr. Robert W. Bartlett, St. Louis; Dr. William A. Bloom, Fayette; Dr. Robert C. Haynes, Marshall; and Dr. Wendell G. Scott, St. Louis.

Dr. Nicholas Kamakas, St. Louis, has been installed

Continued on page 74

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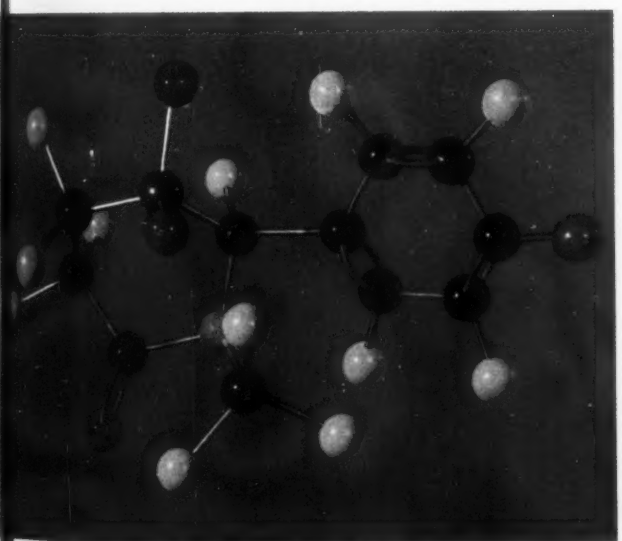
***Potent* MUSCLE RELAXANT**

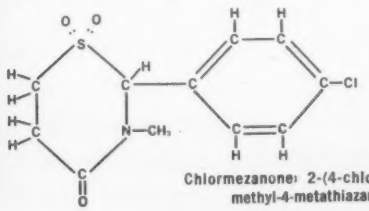
***...Equally effective as a* TRANQUILIZER**

***tran-qui-lax-ant** (tran'kwi-lak'sant) [< L. tranquillus, quiet; L. laxare, to loosen, as the muscles]



Trancopal, a major development of Winthrop research, is a new orally administered nonhypnotic central relaxant and tranquilizer. It relieves muscle spasm in a variety of musculoskeletal and neurologic conditions and also exerts a marked tranquilizing effect in anxiety and tension states.

Unrelated chemically to any other drug in current use, Trancopal offers a completely new major chemical contribution to therapeutics.



Chlormezanone: 2-(4-chlorophenyl)-3-methyl-4-metathiazanone-1-dioxide

Thoroughly evaluated clinically...

Clinical studies of 4092 patients by 105 physicians[1] have demonstrated that Trancopal often is effective when other drugs have failed. From these studies it is evident that Trancopal can provide more help for a greater number of tense, spastic, and/or emotionally upset patients than can any other chemotherapeutic agent in current use.

In musculoskeletal conditions[1]

effective in **91%** of patients

INDICATIONS

Low back pain (lumbago)
Bursitis
Osteoarthritis
Fibrositis
Myositis
Postoperative myalgias
Neck pain (torticollis)
Rheumatoid arthritis
Disk syndrome
Joint disorders (ankle sprain, tennis elbow, etc.)

By relieving muscle spasm and pain, Trancopal permits early and active purposeful exercise and physical therapy to accomplish maximal benefits for rapid recovery.

Trancopal

Dosage: One Caplet (100 mg.) orally three or four times daily. Relief of symptoms occurs in fifteen to thirty minutes and lasts from four to six hours.

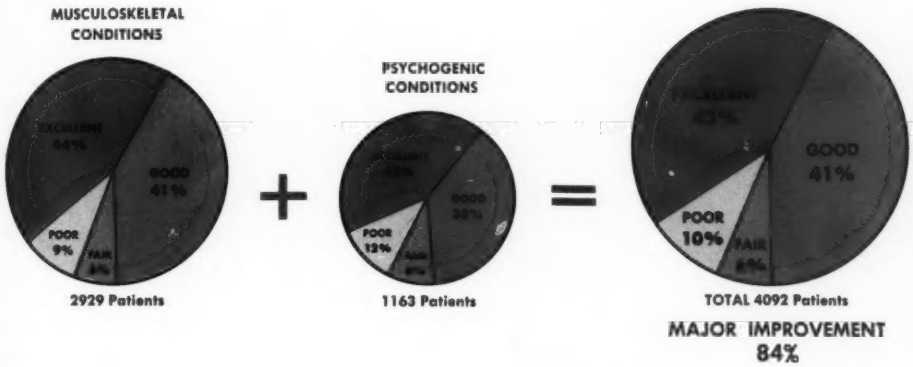
In anxiety and tension states[1]

effective in 88% of patients

INDICATIONS

Anxiety and tension states	Dysmenorrhea
Premenstrual tension	Asthma
Emphysema	Angina pectoris

Because of its exceptional calmative property, Trancopal "...allows the patient to use his energies in a more productive manner in overcoming his basic problem."[2]



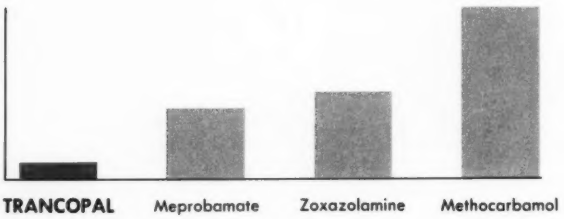
Of the total patients treated, Trancopal produced excellent results in 43 per cent, good results in 41 per cent, fair results in 6 per cent, and poor results in 10 per cent.

Better tolerated and safer than older drugs[3]

With Trancopal there is no clouding of consciousness, no euphoria or depression. Even in high dosage, there is no perceptible soporific effect. Because it does not irritate gastric mucosa, it can be taken without regard to mealtimes. Administration does not hamper work — or play. There are no known contraindications. Blood pressure, pulse rate, respiration and digestive processes are unaffected by therapeutic dosage.
Toxicity is extremely low. And Trancopal has a lower incidence of side effects than has zoxazolamine, methocarbamol or meprobamate.

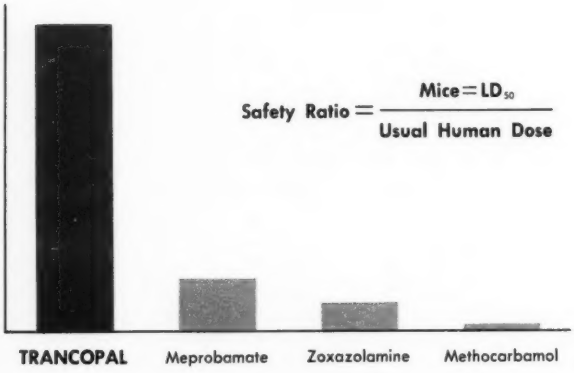
Comparison with 3 widely used central relaxants

When compared with three widely used central relaxants for activity, safety and clinical effectiveness, Trancopal offers definite desirable advantages.



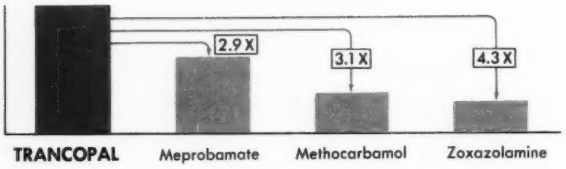
for activity

In the usual human dose, Trancopal is four to ten times as potent per milligram.



for safety

Comparative pharmacologic tests showed that Trancopal is up to thirteen times as safe or up to thirteen times less toxic. The measure of safety was the LD_{50} in mice/usual human dose.



for clinical effectiveness

A clinical comparison in low back pain, torticollis, bursitis and anxiety states showed that Trancopal is up to four times as effective. Each of the 40 patients received all four drugs in random rotation for several days. Although each of the four gave some relief, only the one providing the most effective relief was recorded.

Supplied: Trancopal Caplets® (scored) 100 mg., bottles of 100.

References: 1. Cooperative Study, Department of Medical Research, Winthrop Laboratories. • 2. Gans, S.E.: To be published. • 3. Lichtman, A.L.: Kentucky Acad. Gen. Pract. J. 4:28, Oct., 1958.

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Continued from page 72

as President of the Greek Professional and Cultural Association.

Dr. Frank R. Bradley, St. Louis, Director of Barnes Hospital, has been named a life member of the American Hospital Association, a designation conferred on members of 30 years standing.

Dr. Robert I. Pfeffer, St. Joseph, has been elected to the Board of Directors of the Missouri Association for Mental Health for a term expiring in October 1961.

Dr. John C. Murphy, St. Louis, has been appointed Acting Health Commissioner of St. Louis County.

New officers of the South Central Counties Medical Society include: Dr. Joe Spears, Cabool, President; Dr. Harold Miller, Willow Springs, President-Elect; and Dr. Rollin H. Smith, West Plains, Secretary.

The St. Louis County Medical Society has elected as its officers: Dr. Robert C. Kingsland, Clayton, President; Dr. Joseph B. Kendis, St. Louis, President-Elect; Dr. William S. Brown, St. Louis, Vice-President; and Dr. B. Todd Forsyth, Secretary, also of St. Louis.

NORTH CAROLINA

Dr. Milford O. Rouse, Dallas, Texas, President of the Southern Medical Association, has appointed the following men to serve as Associate Councilors from North Carolina: Dr. John Robert Bender, Winston-Salem; Dr. James Davis, Durham; Dr. Mac Roy Gasque, Pisgah Forest; Dr. J. Leonard Goldner, Durham; and Dr. Ernest Yount, Winston-Salem.

Dr. C. Hampton Mauzy, Professor of Obstetrics and Gynecology at Bowman Gray School of Medicine, has been installed President of the South Atlantic Association of Obstetricians and Gynecologists. Dr. Mauzy had previously served as President-Elect, Vice-President, and Secretary-Treasurer. He assumed the Presidency

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POSITION WANTED—Radiologist F.A.C.R. presently engaged. Eligible for certification for Radioactive Isotopes. Desires location in Georgia, Alabama, or Mississippi, in a community not to exceed twenty thousand which will not require entire time. Would not mind serving two communities. Compensation in proportion to services rendered. Personal interview desired. Contact HF, c/o SMJ.

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at the Association's recent annual meeting in Roanoke, Virginia. Dr. Mauzy is also Chairman of the Section on Obstetrics of the Southern Medical Association.

Dr. James Harrill, Professor of Otolaryngology, Bowman Gray School of Medicine, has been re-elected Secretary of the Southern Section of the American Laryngological, Rhinological and Otological Society.

Dr. Robert H. Wagner, Assistant Professor of Pathology in Pathological Chemistry and Assistant Professor of Biochemistry and Nutrition, University of North Carolina School of Medicine, has been named a Senior Research Fellow by the U. S. Public Health Service.

Dr. Charles A. Bream and Dr. William H. Sprunt, Associate Professors in the Department of Radiology, University of North Carolina School of Medicine, have been elected Fellows in the American College of Radiology.

Dr. Angus C. Randolph, Associate Professor of Psychiatry, Bowman Gray School of Medicine, has been appointed by Governor Luther H. Hodges to a four year term on the reactivated Medical Advisory Committee to the State Hospitals Board of Control. The committee will advise the board on all phases of the state's mental hospital program.

Dr. Davis Gordon Sharp, Professor of Biophysics in the Department of Bacteriology, University of North Carolina School of Medicine, has been named President-Elect of the Electron Microscope Society of

Continued on page 77

Specific immunizing antigen (chick embryo origin) active against various isolated virus strains. Effectively prevents or modifies mumps in children and adults.

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The New Patient *(no previous antidiabetic therapy)*

1. Initial daily dose 500 mg. (2 tablets of 250 mg. each) with breakfast.

2. In elderly patients, initial dose 250 mg. (1 tablet) daily.

3. CONTROL PERIOD

(a) If blood sugar reaches normal levels after three to seven days, or if glycosuria disappears, lower daily dose of 500 mg. to a level between 250 mg. (1 tablet) and 375 mg. (1½ tablets of 250 mg.) with breakfast daily. In elderly patients, dosage may be reduced to as low as 100 mg.

(b) If hyperglycemia or glycosuria persists or develops, increase the daily dose from 500 mg. to 625 mg. (2½ tablets of 250 mg.) with breakfast daily. In elderly patients, dosage should be increased from 250 mg. according to patient response.

(c) Continue weekly adjustments during first month of therapy until maintenance dose has been established. Adjustments below 250 mg. daily are best made in steps of 100 mg. (one 100 mg. tablet). The maintenance dose may occasionally be as low as 100 mg. (one 100 mg. tablet daily) or, rarely, as high as 1.0 Gm. (four 250 mg. tablets) daily. Do not exceed daily dose of 1.0 Gm.

Transfer of Patient from Insulin

1. If patient is taking 40 or less units of insulin daily and gives no history of severe or "brittle" diabetic response, discontinue insulin and replace with DIABINESE as in The New Patient.

2. Complete control period as for The New Patient. Priming ("loading") doses should not be used.

3. If patient is taking more than 40 units of insulin daily, or shows evidence of severe or brittle diabetes, reduce insulin dose by 50 per cent and initiate DIABINESE therapy as for The New Patient. Further reduction of insulin dosage depends on patient response.

Transfer of Patient from Other Oral Medication

Where less than satisfactory control has been achieved with other oral medication, or where a change to once-a-day dosage is desired, DIABINESE may be successfully substituted. Such a transfer may be made by discontinuing previous oral medication, substituting DIABINESE, and continuing control period as for The New Patient. Avoid priming doses.

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Continued from page 75

America. Dr. Sharp has been a pioneer in the development of the electron microscope as a tool for the study of viruses. He has also made many major advances in measuring what may be seen by microscopes or in "quantitating viruses."

Drs. Jefferson E. White, Jr., Robert L. Green, Jr., and Ernest W. Chick of the Durham Veterans Administration Hospital and Duke Medical Center are among a number of outstanding young doctors over the United States who have been selected to participate in the VA Clinical Investigators Program.

Dr. Carl Anderson, Associate Professor of Biochemistry and Assistant Dean for Student Affairs, University of North Carolina School of Medicine, has been elected a Fellow of the American Association for the Advancement of Science.

OKLAHOMA

Dr. Milford O. Rouse, Dallas, Texas, President of the Southern Medical Association, has appointed the following men to serve as Associate Councilors from Oklahoma: Dr. Walter E. Brown, Tulsa; Dr. J. Hoyle Carlock, Ardmore; Dr. Tom S. Gafford, Jr., Muskogee; Dr. J. Wendall Mercer, Enid; and Dr. E. C. Mohler, Ponca City.

Newcomers to the faculty of the University of Oklahoma Medical Center include: Dr. Floyd S. Cornelison, Jr., Assistant Professor of Psychiatry; Dr. Max A. Glaze, Clinical Assistant in Psychiatry; Dr. Stanley M. Kemler, Instructor in Psychiatry; Dr. Lucius Waites, Jr., Assistant Professor of Pediatrics and Assistant Professor of Neurology; Dr. Doman K. Keele, Assistant Professor of Pediatrics; and Dr. Frances G. Felton, Assistant Professor of Research Microbiology.

The Postgraduate School of the University of Oklahoma Medical Center will hold its Fifth Annual Surgery, Radiology, Pathology Symposium May 8 and 9. The Symposium this year will be *Diagnosis and Treatment of Thyroid Diseases.*

Dr. Harlan Thomas, Tulsa, was recently chosen President-Elect of the Tulsa Academy of General Practice.

SOUTH CAROLINA

Dr. Milford O. Rouse, Dallas, Texas, President of the Southern Medical Association, has appointed the following men to serve as Associate Councilors from South Carolina: Dr. John M. Fleming, Spartanburg; Dr. R. W. Hanckel, Charleston; Dr. D. Strother Pope, Columbia; Dr. Thomas F. Stanfield, Anderson; and Dr. J. Howard Stokes, Florence.

Dr. Joseph P. Cain, Jr., Mullins, has been appointed to the Board of Trustees of the Medical College of South Carolina at Charleston by Governor George Bell Timmerman. He succeeds the late Dr. Frank L. Martin.

Dr. John M. Fleming, Director of the Cancer Clinic at Spartanburg General Hospital, and Associate Councilor to the Southern Medical Association, has been

Continued on page 80

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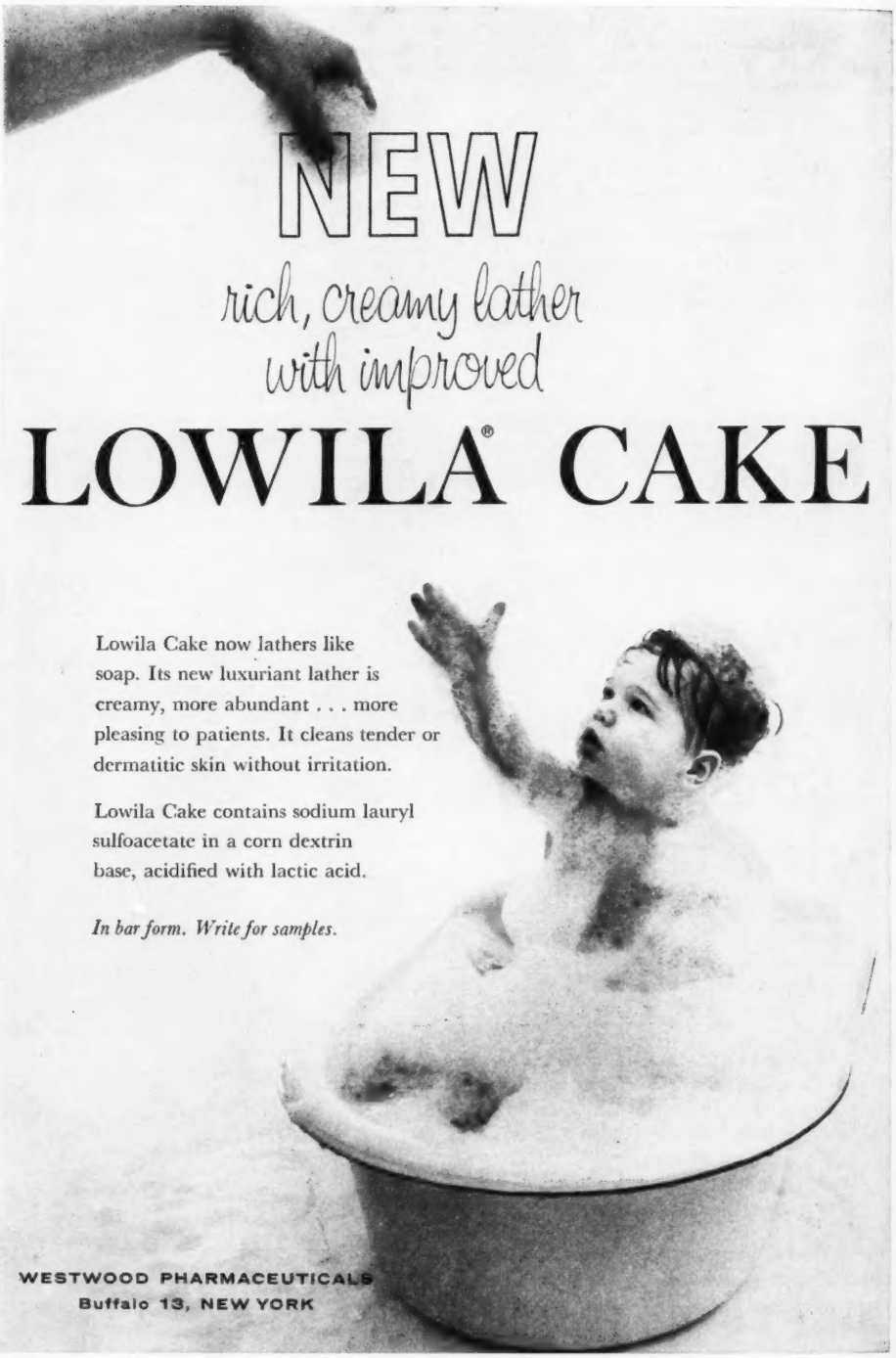
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Each teaspoonful (5 cc.) contains:

l-Lysine HCl	300 mg.
Vitamin B_{12} Crystalline	25 mcgm.
Thiamine HCl (B_1)	10 mg.
Pyridoxine HCl (B_6)	5 mg.
Ferric Pyrophosphate (Solution)	250 mg.
Iron (as Ferric Pyrophosphate)	30 mg.
Sorbitol	3.5 Gm.

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Continued from page 77

elected to receive the 1958 citation and medallion presented annually by the American Cancer Society's South Carolina Division to the most outstanding person in the state in the field of cancer control for that year. The award is the highest honor bestowed by the division.

Dr. J. A. White was recently honored by the Easley Exchange Club by being named Easley's "Citizen of the Year" for 1958.

TENNESSEE

Dr. Milford O. Rouse, Dallas, Texas, President of the Southern Medical Association, has appointed the following men to serve as Associate Councilors from Tennessee: Dr. B. F. Byrd, Jr., Nashville; Dr. William A. Garrott, Cleveland; Dr. Frank Tullis, Memphis; and Dr. Charles P. Wofford, Johnson City.

Dr. Frank L. Roberts, Associate Dean at the University of Tennessee Medical School, left in March to go to Iran for two years as a Consultant in Medical Education at the University of Shiraz. Dr. Roberts, who also teaches preventive medicine, went to the English-speaking university in southern Iran under auspices of the International Co-operation Administration.

Dr. Davis S. Carroll, Professor of Radiology, University of Tennessee Medical School, has been appointed head of the Department succeeding Dr. Charles

Continued on page 82

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Opportunities in general practice for men who have completed one year internships. Starting salary $13,800.

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Positions also available for Ophthalmologist, Internist, and Pathologist. Board certified or eligible.

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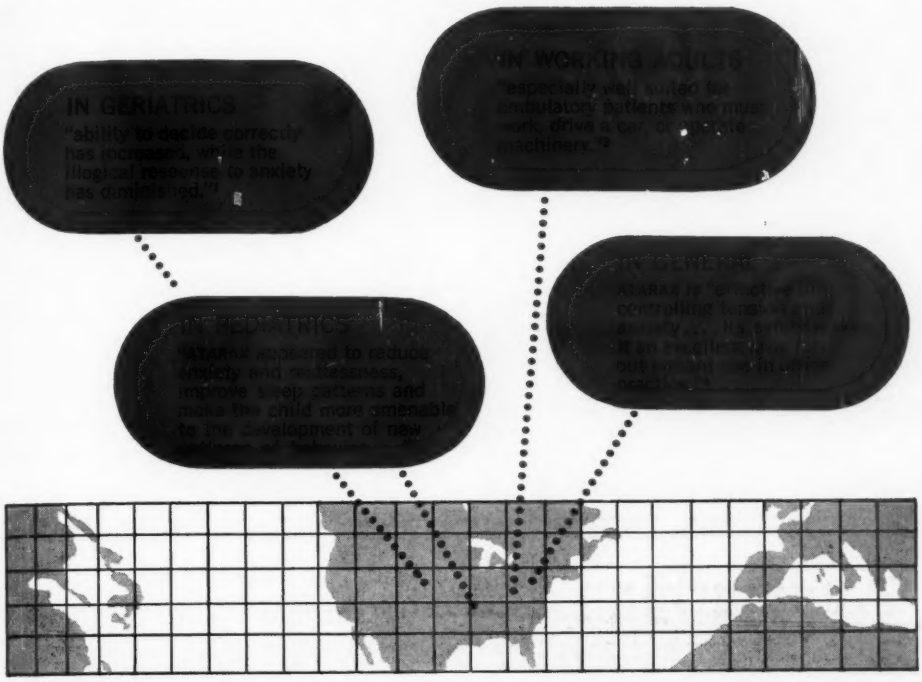
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	Syrup	3-6 years, one tsp. t.i.d. over 6 years, two tsp. t.i.d.
For adult tension and anxiety	25 mg. tablets	one tablet q.i.d.
	Syrup	one tbsp. q.i.d.
For severe emotional disturbances	100 mg. tablets	one tablet t.i.d.
For adult psychiatric and emotional emergencies	Parenteral Solution	25-50 mg. (1-2 cc.) intramuscularly, 3-4 times daily, at 4-hour intervals. Dosage for children under 12 not established.

Supplied: Tablets, bottles of 100. Syrup, pint bottles. Parenteral Solution, 10 cc. multiple-dose vials.

References: 1. Smigel, J. O., et al.: J. Am. Ger. Soc., in press. 2. Freedman, A. M.: Pediat. Clin. North America 5:573 (Aug.) 1958. 3. Ayd, F. J., Jr.: New York J. Med. 57:1742 (May 15) 1957. 4. Menger, H. C.: New York J. Med. 58:1684 (May 15) 1958. 5. Coirault, M., et al.: Presse méd. 64:2239 (Dec. 26) 1956. 6. Bayart, J.: Presented at the International Congress of Pediatrics, Copenhagen, Denmark, July 22-27, 1956.

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Continued from page 80

Hunter Heacock, who resigned. Dr. Heacock will continue as Professor of Radiology.

Newly elected officers of the St. Thomas medical staff are the following Nashville physicians: Dr. Joe Anderson, President-Elect; Dr. Robert McCracken, President; and Dr. Russell T. Birmingham, Secretary-Treasurer.

Dr. J. Wesley McKinney, Memphis, has been named President of the medical staff at the Memphis Eye, Ear, Nose and Throat Hospital. Other new officers are Dr. Alice Deutsch, Vice-President, and Dr. Eugene Vacarro, Secretary.

Dr. Ralph H. Shilling, Gatlinburg, has been named Health Officer for Sevier County.

Dr. Albert B. Qualls, Livingston, has been named Tennessee State Chairman for the National Foundation for Muscular Dystrophy.

Drs. John Lentz, O. N. Bryan, John Lee, R. W. Billington, L. J. Caldwell and H. P. Rieger, all of Nashville, were recently presented pins in recognition of fifty years in the practice of medicine. The presentations were made by Dr. James C. Gardner of Nashville.

Dr. W. R. Sullivan, Bells, has been named President of the Crockett County Unit of the American Cancer Society.

Dr. L. M. Donalson, Fayetteville, has been named President-Elect of the Lincoln County Medical Society.

Continued on page 84

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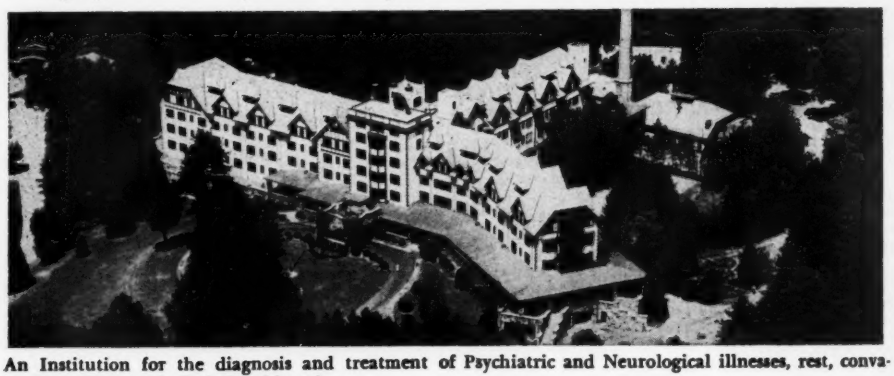

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... because Cobalt is the nucleus of the B_{12} molecule — must be present for intestinal bacterial flora to produce B_{12} — is a proven effective catalyst for increasing Hb content and formation of erythrocytes. And, Cobalt in the recommended Li-Betaron dosage is safe, even for infants.

... because Li-Betaron provides immediately-usable B_{12} until normal intestinal synthesis can be stimulated by Cobalt.

DOSAGE

ADULTS — 1 tablespoonful twice daily after meals.
6 to 12 years — 1 or 2 teaspoonfuls twice daily after meals.
1 to 6 years — ½ to 1 teaspoonful twice daily after meals.
INFANTS — 10 to 20 drops (5 to 10 minims) in milk.

SUPPLIED—In pint and gallon bottles.

EACH 30cc CONTAINS

Vitamin B_{12} Crystalline	25 mcg.
Elemental Cobalt (as Cobalt Chloride)	1.5 mg.
Liver Concentrate	1 Gm.
Ferric Ammonium Citrate (10 MDR) (Iron 100 mg.)	572 mg.
Panthenol	5 mg.
Thiamine HCl (18 MDR)	18 mg.
Riboflavin (3 MDR)	6 mg.
Nicotinamide	60 mg.
Pyridoxine HCl	2 mg.

In pernicious anemia, Li-Betaron Elixir is recommended only as a supplement to parenteral use of Liver Injection USP, or equivalent.

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Continued from page 82

Dr. Carl T. Kirchmaier, Nashville, has been named Chairman of the 1959 Heart Fund Campaign for Middle Tennessee.

Dr. Ralph O. Rychener, Memphis, was re-elected President of the National Foundation for Eye Care by the Foundation's Board of Trustees at their annual meeting.

Dr. Harold B. Boyd, Professor of Orthopedic Surgery, has been appointed head of the Department of Orthopedic Surgery at the University of Tennessee School of Medicine, succeeding Dr. James Spencer Speed. Dr. Speed has resigned his administrative duties but will continue as Professor in the Department.

TEXAS

Dr. Robert D. Moreton, Fort Worth, College Chancellor elected by the Radiological Society of North America, has been installed as President of the Tarrant County Medical Society. Dr. Moreton has been a very active member of the Southern Medical Association since 1948, now serving in the capacity of Councilor from Texas, Vice-Chairman of the Council, member of the Executive Committee, and Chairman of the Insurance Committee. He has also served as Secretary, Vice-Chairman, and Chairman of the Section on Radiology.

Dr. Milford O. Rouse, Dallas, President of the

Continued on page 88

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A private hospital for diagnosis and treatment of psychiatric and neurological patients. Hospital and out-patient services.

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Selective

Does not interfere with autonomic function
Does not impair mental efficiency,
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Has not produced hypotension,
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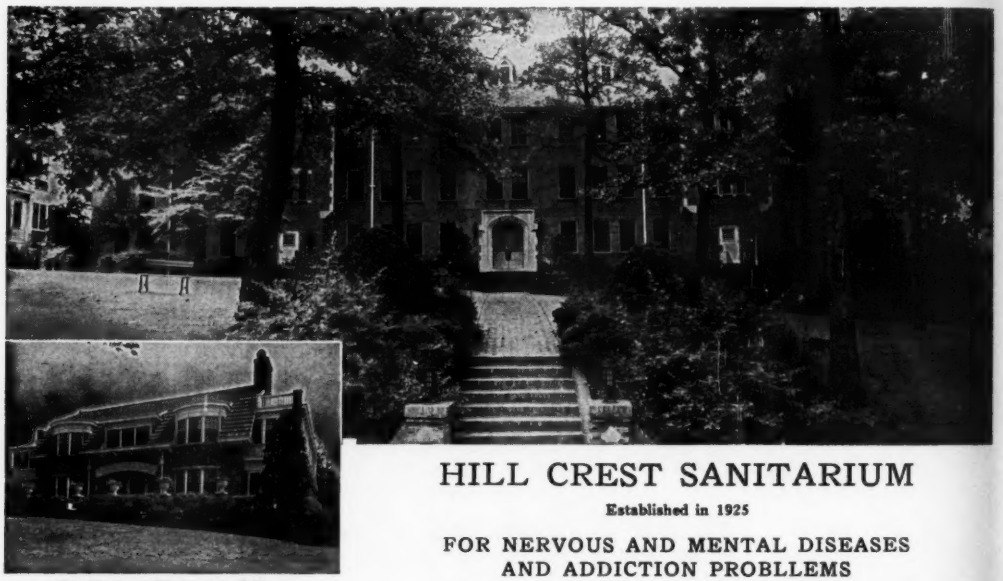

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ORGANIDIN retains potency indefinitely while Lugol's solution and potassium iodide solution change composition on standing. ORGANIDIN is readily and rapidly absorbed. ORGANIDIN dosage can begin at therapeutic level—effect is smooth and sustained. Since the iodine in ORGANIDIN is *organically bound* it is well tolerated, more so than potassium iodide,[1] and permits more prolonged, uninterrupted therapy.[2] Whenever you prescribe iodine therapy, prescribe ORGANIDIN solution or tablets—unexcelled and inexpensive therapy. *Indications:* Expectorant in asthma, bronchitis, and similar forms of pulmonary congestion, goiter prophylaxis, and as an adjunct in simple goiter and thyrotoxicosis. For complete dosage and supply information, see page 847 of your Physicians' Desk Reference. *References:* 1. Seltzer, A.: M. Ann. District of Columbia 26:17, 1957. 2. Slaughter, D.: South Dakota J. Med. & Pharm. 1:125, 1947.

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SANITARIUM

For the diagnosis and treatment of nervous and mental disorders, and addiction to alcohol and drugs.

Established 1907

NASHVILLE, TENNESSEE

Continued from page 84

Southern Medical Association, has appointed the following men to serve as Associate Councilors from Texas: Dr. William M. Ashe, Dallas; Dr. Nicholas C. Hightower, Temple; Dr. Robert W. Kimbro, Cleburne; Dr. Thomas L. Royce, Houston; and Dr. Franklin W. Yeager, Corpus Christi.

The Twentieth Annual Meeting of the Southwest Allergy Forum will be held April 26, 27, and 28, at the Shamrock Hilton Hotel in Houston.

The new officers of the Texas Academy of General Practice are: Dr. Charles E. Oswalt, Jr., Fort Stockton, President; Dr. Jack M. Partain, San Antonio, Vice-President and Chairman of the Board of Directors; Dr. E. Sinks McLarty, Galveston, President-Elect; and Dr. L. W. Johnson, Houston, Treasurer.

VIRGINIA

Dr. Milford O. Rouse, Dallas, Texas, President of the Southern Medical Association, has appointed the following men to serve as Associate Councilors from Virginia: Dr. Charles M. Caravati, Richmond; Dr. Charles E. Davis, Jr., Norfolk; Dr. T. Dewey Davis, Richmond; Dr. Douglas S. Divers, Pulaski; and Dr. Malcolm Harris, West Point.

The following County Medical Societies have elected officers:

Halifax County. Dr. George Lee Wilkinson, South

Continued on page 92

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Each capsule contains:	
Vitamin A	5,000 U.S.P. Units
Vitamin D	500 U.S.P. Units
Vitamin B_{12} with AUTRINIC® Intrinsic Factor Concentrate	1 15 U.S.P. Oral Unit
Thiamine Mononitrate (B_1)	5 mg.
Riboflavin (B_2)	5 mg.
Niacinamide	15 mg.
Folic Acid	1 mg.
Pyridoxine HCl (B_6)	0.5 mg.
Ca Pantothenate	5 mg.
Choline Bitartrate	50 mg.
Inositol	50 mg.
Ascorbic Acid (C)	50 mg.
Vitamin E (as tocopheryl acetates)	10 I.U.
l-Lysine Monohydrochloride	25 mg.
Rutin	25 mg.
Ferrous Fumarate	30 mg.
Iron (as Fumarate)	10 mg.
Iodine (as KI)	0.1 mg.
Calcium (as $CaHPO_4$)	157 mg.
Phosphorus (as $CaHPO_4$)	122 mg.
Boron (as $Na_2B_4O_7.10H_2O$)	0.1 mg.
Copper (as CuO)	1 mg.
Fluorine (as CaF_2)	0.1 mg.
Manganese (as MnO_2)	1 mg.
Magnesium (as MgO)	1 mg.
Potassium (as K_2SO_4)	5 mg.
Zinc (as ZnO)	0.5 mg.

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- in postnasal drip
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Relief with Triaminic is prompt and prolonged because of this special timed-release action . . . beneficial effect starts in minutes, lasts for hours.

first—the outer layer dissolves within minutes to produce 3 to 4 hours of relief
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Each* TRIAMINIC *Tablet provides:

Phenylpropanolamine HCl	50 mg.
Pheniramine maleate	25 mg.
Pyrilamine maleate	25 mg.

One-half of this formula is in the outer layer, the other half is in the core.

Dosage: One tablet in the morning, mid-afternoon and in the evening, if needed.

Triaminic®

Also available: For the occasional patient who requires only half dosage: timed-release TRIAMINIC JUVELETS. Each Juvelet is equivalent to ½ of a Triaminic Tablet.

For those patients who prefer liquid medication: TRIAMINIC SYRUP. Each 5 ml. tsp. of this palatable syrup is equivalent to ¼ of a Triaminic Tablet.

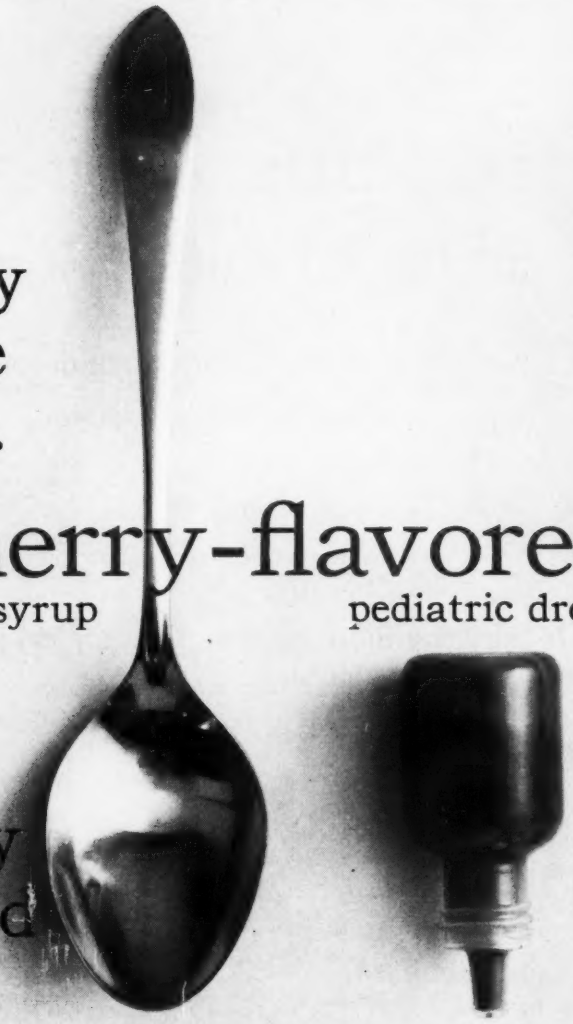
SMITH-DORSEY • a division of The Wander Company • Lincoln, Nebraska • Peterborough, Canada

as they like it...

cherry-flavored

syrup

pediatric drops



as they need it...

ACHROMYCIN® V

Tetracycline with Citric Acid Lederle

- broad spectrum control of more than 90 per cent of antibiotic-susceptible infections seen in general practice[1]
- fast, high concentrations in body fluids and tissues
- no irreversible side effects reported, excellently tolerated
- readily miscible in water, juices, formula.

ACHROMYCIN V: 10 cc. plastic dropper bottle for precise dosage; 100 mg. per cc. (20 drops). *Dosage:* one drop per pound body weight per day.

ACHROMYCIN V Syrup: Each teaspoonful (5cc.) contains equiv. 125 mg. tetracycline HCl. Bottles of 2 and 16 fl. oz. *Dosage:* at 45 lbs., one teaspoonful 4 times daily; adjust for other weights.

1. ***Based on six-month National Physicians Survey.***

Lederle LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

even if your patient is a boom rat

*logger who rafts logs in a "boom"

he'll be pulling down his pay again soon thanks to

(PARAFLEX® + TYLENOL®)

for muscle relaxation *plus* analgesia

and in arthritis

prescribe PARAFON in low back pain —sprains—strains—rheumatic pains

Each PARAFON tablet contains:
PARAFLEX Chlorzoxazone‡ . . . . . 125 mg.
A most effective oral muscle relaxant
TYLENOL Acetaminophen . . . . . 300 mg.
The preferred analgesic for painful musculoskeletal disorders

Dosage: Two tablets t.i.d. or q.i.d.

Supplied: Tablets, scored, pink, bottles of 50.

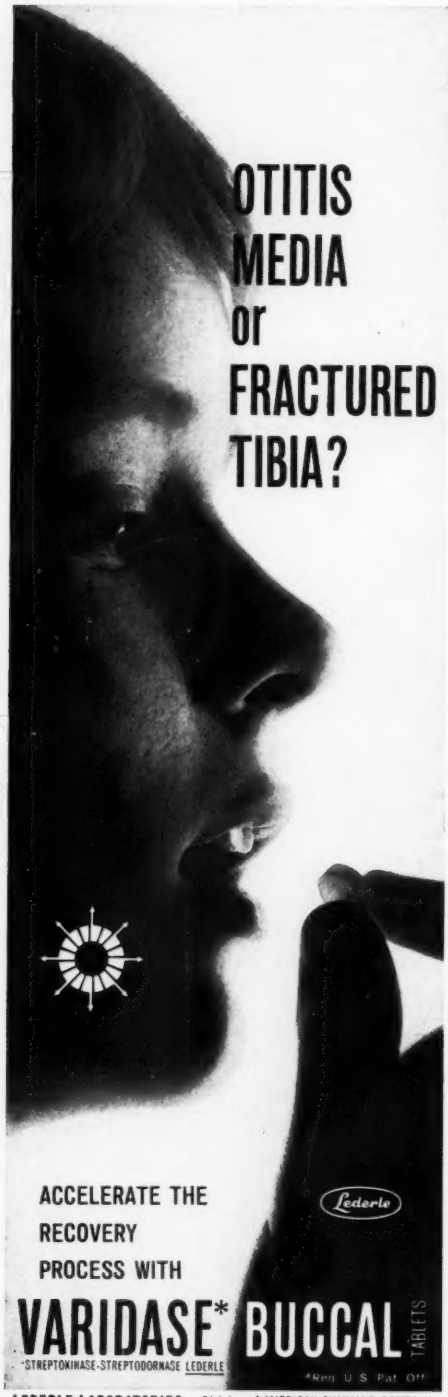
Each PARAFON WITH PREDNISOLONE tablet contains: PARAFLEX® Chlorzoxazone‡ 125 mg., TYLENOL® Acetaminophen 300 mg., and prednisolone 1.0 mg.

Supplied: Tablets, scored, buff colored, bottles of 36.

Precautions: The precautions and contraindications that apply to all steroids should be kept in mind when prescribing PARAFON WITH PREDNISOLONE.

McNeil Laboratories, Inc • Philadelphia 32, Pa.

†Trademark ‡U. S. Patent Pending



LEDERLE LABORATORIES, a Division of AMERICAN CYANAMID COMPANY,
Pearl River, New York

Continued from page 88

Boston, President; Dr. Warren C. Hagood, Clover, Vice-President; and Dr. Lucien D. Roberts, South Boston, Secretary-Treasurer.

Fairfax County. Dr. Thomas O'Brien, President; Dr. Carl P. Parker, Jr., President-Elect; Dr. Peter Soyster, Vice-President; Dr. John Prominski, Secretary; and Dr. Frances Ayres, Treasurer. All officers are from Falls Church.

Northern Virginia. Dr. George Waterman, Woodford, President; Dr. Bradford Bennett, Winchester, Vice-President; and Dr. Dennis P. McCarty, Front Royal, Secretary-Treasurer.

Arlington County. Dr. Stephen J. Sheeny, President; Dr. Robert L. Norment, President-Elect; Dr. Michael A. Puzak, Vice-President; Dr. Howard O. Mott, Secretary; and Dr. James H. Stallings, Treasurer.

Dr. Alfred P. Jones, Roanoke, has been awarded the J. Shelton Horsley Award for outstanding work in cancer control in Virginia. This is the eleventh time the award has been given. Dr. Jones is a member of the staff of Jefferson Hospital and has long been active in cancer control. He is a former President of the Virginia Division of the Cancer Society.

Dr. William P. Frazer, Hamilton, has been elected Chief of Staff of the Loudoun Hospital, succeeding Dr. Joseph M. Rogers. Dr. Keith M. Oliver, Purcellville, is Vice-Chief and Dr. Earl E. Virts, Jr., Leesburg, Secretary.

The citizens of Louisa County have dedicated a picnic area in honor of Dr. E. Barbour Pendleton, the county's oldest practicing physician. The area is called "Pendleton Wayside."

Dr. R. L. Brickhouse has been elected President of the Virginia Baptist Hospital, Lynchburg; Dr. Earl T. Owen, Vice-President; and Dr. Edwin B. Vaden, Secretary.

WEST VIRGINIA

Dr. Milford O. Rouse, Dallas, Texas, President of the Southern Medical Association, has appointed the following men to serve as Associate Councilors from West Virginia: Dr. Albert C. Esposito, Huntington; Dr. W. E. Hoffman, Charleston; Dr. Harold Howell, Madison; Dr. W. F. Shirkey, Charleston; and Dr. Walter E. Vest, Huntington.

Dr. Chauncey B. Wright, Huntington, has been elected President of the West Virginia Cancer Society, succeeding Dr. T. P. Mantz of Charleston.

Dr. E. A. Litsinger, Charleston, has accepted appointment as Clinical Director of Spencer State Hospital.

Dr. W. T. Booher, Jr., Wellsburg, has been appointed by the Brooke County Court as part-time Health Officer and as Coroner to fill the vacancies created by the death of Dr. C. R. Megahan.

Dr. William R. McCune, Martinsburg, has been reelected President of the Eastern Panhandle Medical Society. Other officers include: Dr. George S. Appleby, First Vice-President; Dr. C. V. Townsend, Second Vice-President; and Dr. E. Andrew Zepp, Secretary-Treasurer.

IN OFFICE SURGERY

ELECTIVE AND TRAUMATIC

use XYLOCAINE *first...*
as a local anesthetic
or a topical anesthetic

SWAB SPRAY INFILTRATION NERVE BLOCK

Xylocaine HCl solution, the versatile anesthetic for general office surgery, relieves pain promptly and effectively with adequate duration of anesthesia. It is safe and predictable. Local tissue reactions and systemic side effects are rare. Supplied in 20 cc. and 50 cc. vials; 0.5%, 1% and 2% without epinephrine and with epinephrine 1:100,000; also in 2 cc. ampules; 2% without epinephrine and with epinephrine 1:100,000.

XYLOCAINE® HCl SOLUTION
(brand of lidocaine*)

Astra Pharmaceutical Products, Inc., Worcester 6, Mass., U.S.A.

SEE PDR

*U.S. PAT. NO. 2,441,498 MADE IN U.S.A.

it started as a "cold"...

to prevent the sequelae of u.r.i. ... and relieve the symptom complex

ACHROCIDIN®

Tetracycline-Antihistamine-Analgesic Compound Lederle

Pneumonitis, otitis, tonsillitis, adenitis, sinusitis or bronchitis develops as a serious bacterial complication in about one in eight cases of acute upper respiratory infection.[1] To protect and relieve the "cold" patient... ACHROCIDIN.

Usual dosage: 2 tablets or teaspoonfuls q.i.d. (equiv. 1 Gm. tetracycline). Each TABLET contains: ACHROMYCIN® Tetracycline (125 mg.); phenacetin (120 mg.); caffeine (30 mg.); salicylamide (150 mg.); chlorothen citrate (25 mg.). Also as SYRUP (lemon-lime flavored), caffeine-free.

1. Based on estimate by Van Volkenburgh, V. A., and Frost, W. H.: Am. J. Hygiene 71:122 (Jan.) 1933

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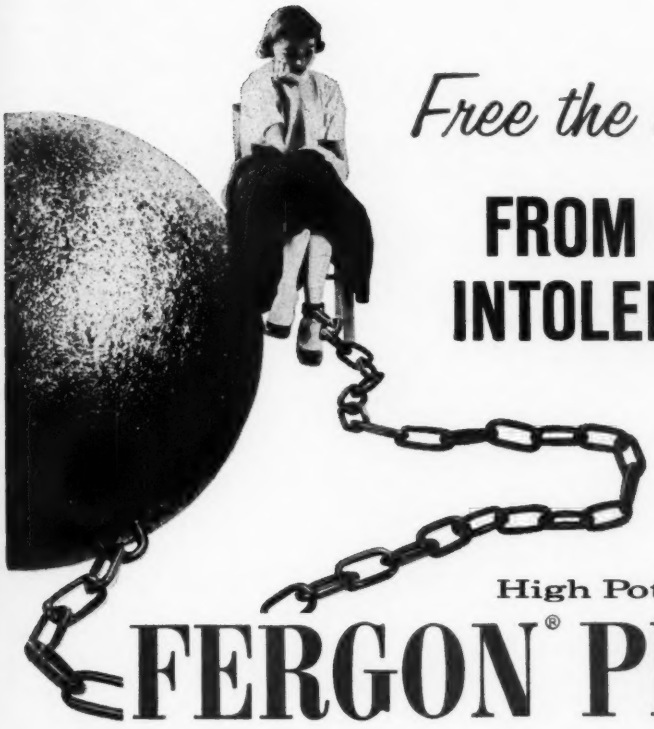


Free the anemic

FROM IRON INTOLERANCE

High Potency

FERGON® PLUS

Improved Caplets®

2 Caplets = 1 U.S.P. oral unit of Anti-Anemia Activity *without* gastrointestinal upset

2 Caplets contain:

Fergon (brand of ferrous gluconate) Iron without Irritation	1000 mg.
Vitamin B_{12} with Intrinsic Factor Concentrate U.S.P.	1 unit (oral)
Folic acid	3 mg.
Ascorbic acid	150 mg.

Highest Hemoglobin Response

No Nausea
No Abdominal Cramps
No Constipation
No Diarrhea
in approximately 90% of patients

Therapeutic dose: Only 2 Fergon Plus Caplets daily (one before the morning and evening meals).

How Supplied:

Fergon Plus Improved Caplets, bottles of 100 and 500 easy to swallow Caplets.

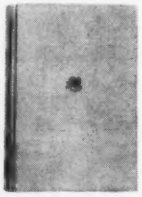
Winthrop LABORATORIES NEW YORK 18, N. Y.

Fergon (brand of ferrous gluconate) and Caplets, trademarks reg. U. S. Pat. Off.

Question:
Why do so many physicians prefer Cafergot and Cafergot P-B for migraine and other recurrent throbbing headaches?

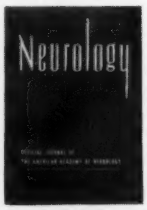
Answers:
By leading clinicians, quoted from their published investigations.

"The highest percentage (83%) of patients with symptomatic relief is obtained by early and adequate administration of ergotamine and caffeine (Cafergot), alone or combined with antispasmodics and/or sedatives (Cafergot P-B)." *(Friedman, A. P.: J.A.M.A. 163: 1111, March 30, 1957.)*



"For those patients in whom nausea and vomiting occur so early in the attack that oral medication cannot be used, rectal administration is sometimes a simple and effective solution. Cafergot suppositories ... and Cafergot P-B suppositories ... are useful additions to the armamentarium." *(MacNeal, P. S., et al.: Management of the Patient with Headache, 1957.)*

"The tablets [Cafergot P-B] were especially useful when the headaches were accompanied by nervous tension and gastrointestinal upset.... Cafergot P-B Tablets constitute an important addition to the treatment of vascular headache." *(Blumenthal, L. S., and Fuchs, M.: Med. Annals District of Columbia 26:175, April 1957.)*



"Symptomatic treatment is essentially one of pharmacotherapy, and the best results have been obtained with the use of ergotamine derivatives, notably a compound of ergotamine and caffeine (Cafergot)." *(Friedman, A. P., von Storch, T. J. C., Merritt, H. H.: Neurology 4:773, Oct. 1954.)*

first choice
for migraine
and other recurrent,
throbbing headaches

CAFERGOT®

CAFERGOT TABLETS
ergotamine tartrate 1 mg., caffeine 100 mg.
Dosage: 2 at first signs of attack; if needed, 1 additional tab. every ½ hour until relieved (max. 6 per attack).

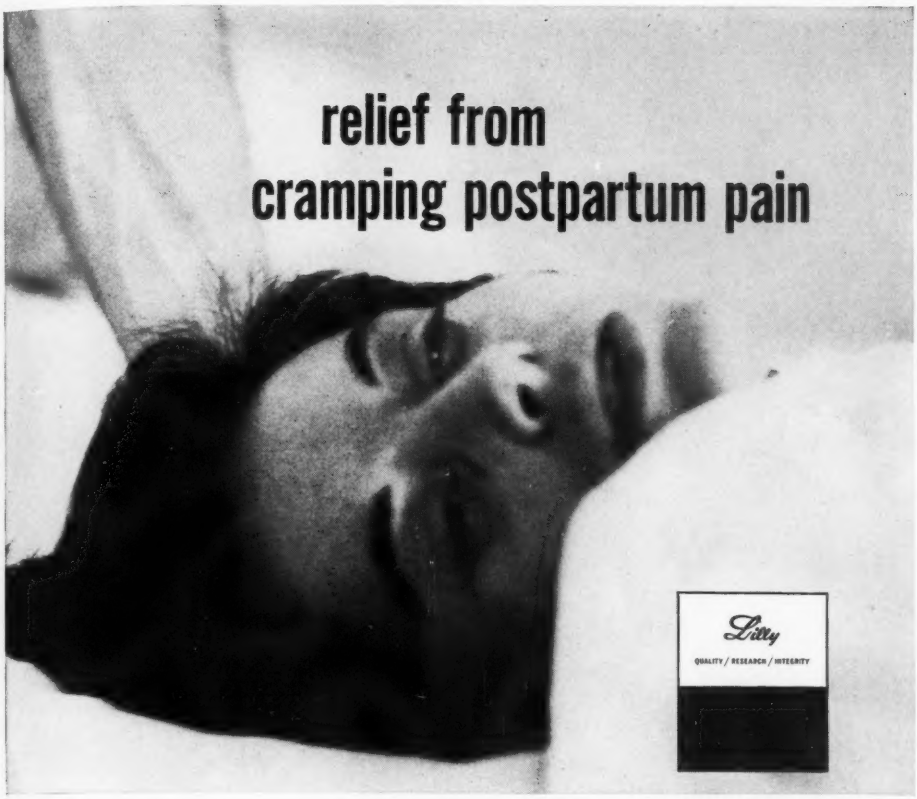
CAFERGOT SUPPOSITORIES
ergotamine tartrate 2 mg., caffeine 100 mg.
Dosage: 1 as early as possible in attack; second in one hour, if needed (max. 2 per attack).

When the headache is associated with nervous tension and G.I. disturbance

CAFERGOT P-B TABLETS
ergotamine tartrate 1 mg., caffeine 100 mg., Bellafoline 0.125 mg., pentobarbital sodium 30 mg.
Dosage: same as Cafergot Tablets.

CAFERGOT P-B SUPPOSITORIES
ergotamine tartrate 2 mg., caffeine 100 mg., Bellafoline 0.25 mg., pentobarbital sodium 60 mg.
Dosage: same as Cafergot Suppositories.

SANDOZ



DARVON® COMPOUND, potent · safe · well tolerated

The clinical usefulness of Darvon® (dextro propoxyphene hydrochloride, Lilly), alone and in combination, has been substantiated by more than a hundred investigators in the treatment of over 6,300 cases. Of 439 postpartum patients, 400 (91.1 percent) obtained effective analgesia; 39 (8.9 percent) did not respond. Six patients experienced some constipation, the only side-effect encountered.

Darvon Compound combines, in a single Pulvule®, the analgesic action of Darvon with the antipyretic and anti-inflammatory benefits of A.S.A.® Compound (acetylsalicylic acid and acetophenetidin compound, Lilly).

Usual dosage for Darvon Compound is 1 or 2 Pulvules three or four times daily; for Darvon, dosage is 32 mg. every four hours or 65 mg. every six hours.

Darvon is available in 32 and 65-mg. Pulvules at pharmacies everywhere.

Darvon® Compound (dextro propoxyphene and acetylsalicylic acid compound, Lilly)

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920201

help prepare your patients for a healthy, active later life

PRESCRIBE

ELDEC

vitamin-mineral-hormone supplement

KAPSEALS®

during their middle years

each KAPSEAL *contains:*

vitamins	
Vitamin A	1,667 Units (0.5 mg.)
Vitamin B_1 mononitrate	0.67 mg.
Ascorbic acid	33.3 mg.
Nicotinamide	16.7 mg.
Vitamin B_2	0.67 mg.
Vitamin B_6	0.5 mg.
Vitamin B_{12} with intrinsic factor concentrate	0.033 USP Unit (oral)
Folic acid	0.1 mg.
Choline bitartrate	6.67 mg.
Pantothenic acid (as the sodium salt)	5 mg.
minerals	
Ferrous sulfate (exsiccated)	16.7 mg.
Iodine (as potassium iodide)	0.05 mg.
Calcium carbonate	66.7 mg.
digestive enzymes	
Taka-Diastase®	20 mg.
Pancreatin	133.3 mg.
protein improvement factors	
l-Lysine monohydrochloride	66.7 mg.
dl-Methionine	16.7 mg.
gonadal hormones	
Methyl testosterone	1.67 mg.
Theelin	0.167 mg.

dosage: One Kapseal three times daily before meals. Female patients should follow each 21-day course with a 7-day rest interval.

packaging: ELDEC Kapseals are available in bottles of 100.

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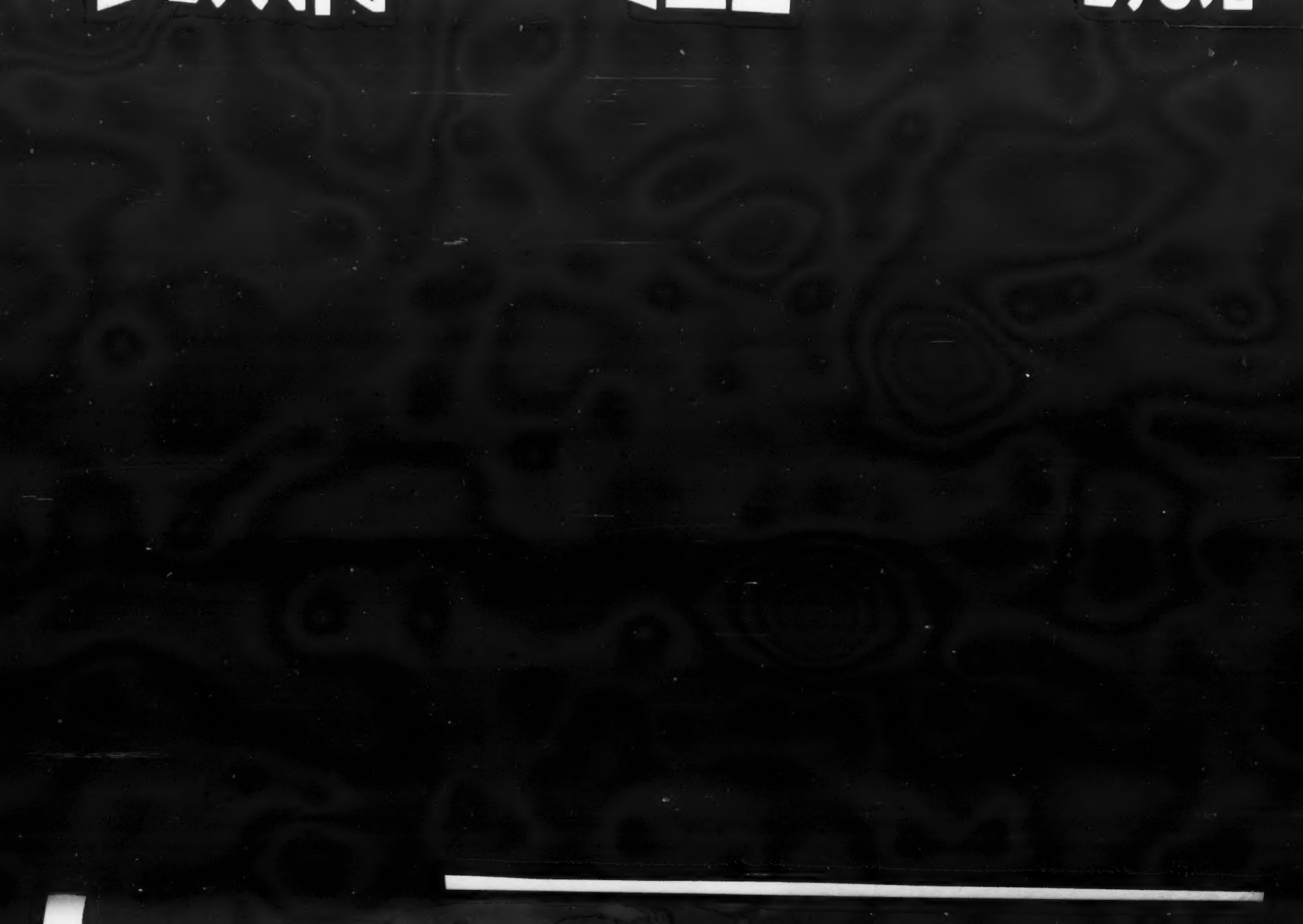
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